The American Journal of Surgery

VOLUME 101 FEBRUARY 1961 NUMBER TWO

EDITORIAL

Infection in the Operating Room

MEASURES to prevent infections in surgical patients have been studied in many parts of the country and reports that deal with various aspects of this problem are appearing frequently in surgical journals. Virtually all wound infections have their inception in the operating room. Concern about the occurrence of bacterial populations that are resistant to antibiotics has stimulated the resurgence of bacteriology in surgery. Many of the reports that have appeared recently are devoted to individual areas that are of particular interest to the investigator. These have included airborne contamination, ultraviolet lights, solutions to disinfect operating room floors, ventilation and special filters, agents for surgical scrubbing of the hands of the team and the operative area, special masks, impervious drapes, carriers of pathogenic organisms among members of the surgical team, contamination from blankets and bedding, and surgical technic. Studies of these areas are important when adapted to the over-all care of the patient and the particular operating suite.

It should be emphasized that many of the studies which are directed toward one or more of these measures are very insular in their application. Although the underlying principles may be generally acceptable, the specific factors may not, because many of the steps necessary to prevent infection depend on physical controls within the institution. Since one hospital varies greatly from another, the modifications in the physical properties may apply to only a particular institution. Consideration of these limitations are pertinent in appraisal of the numerous reports in the literature.

Perhaps the most important result that has emerged from the studies of surgical infections has been the emphasis on surgical technic. It is apparent that the patient must not be weakened unduly by treatment. Inadequate hemostasis and crushing of tissue cannot be counteracted by ultraviolet lights or by antiseptic agents that reduce the bacterial count on the surgeons' hands.

Frequent review of the measures that are being used in the operating rooms are needed. Analysis of the effectiveness of technic must include consideration of housekeeping and maintenance. Failure to keep a vigilant watch may be followed by an epidemic of infections. We have found that actual inspection of the operating rooms and surgical areas of the hospital by a team of surgeons, nurses and administrators has been an effective method of maintaining standards of asepsis and of co-ordinating improvements when indicated. It requires constant and alert supervision by the members of the staff who are responsible for the operating room to see that the necessary precautions are used consistently to protect the patient. *The surgical patient is a weakened host in a potentially dangerous environment.*

Regardless of restrictive steps and physical modifications, ultimate responsibility rests upon the surgeon. The most important factor in the control and prevention of infection is the education of the surgeon—*intern, resident and senior surgical staff*. A review of infections and frank evaluation of their pathogenesis are needed. Study of patients with infection should be made in a constructive manner in an effort to reduce potential hazards in the future.

Repetition is a necessity for indoctrination in the principles of control of infection in surgery.

One of the most interesting facts that has been brought forth by laboratory studies is that a similar bacterial inoculum in several wounds does not uniformly result in clinical infection. Therefore, it is apparent that there must be local factors in the wound which influence the development of infection. This emphasizes the important role of the surgeon's technic. Infection is less likely to develop if the wound is made as unreceptive to bacteria as possible. Since viable tissue resists infection well, while ischemic and necrotic tissue encourage infection, gentle and meticulous handling of tissues is essential.

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SCIENTIFIC PAPERS

Experimental Pulmonary Arterial Hypertension

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DIRECT surgical repair of the most complex cardiac anomalies has been made possible by the use of extracorporeal circulatory devices [1–3]. Technical restoration of normal circulatory pathways can be accomplished in many of these patients. However, there is still a group of patients in whom changes occur in pulmonary vasculature which frustrate recovery even though the offending defect has been corrected.

The significance and pathogenesis of these alterations in the pulmonary vasculature have been described by Edwards [16–19], Heath [30], Dammann [9,11,13], and Muller [42] and their associates.

Since there is good correlation between the hemodynamic characteristics of pulmonary blood flow and microscopic alterations of the pulmonary arteries, the study of experimentally induced pulmonary vascular lesions is worthwhile. The question of whether or not far advanced vascular lesions will improve when the inciting agent is removed is particularly important. The present investigation is comprised of a review of experimental technics and a description of our own investigation. Evidence of regression of advanced pulmonary arterial lesions will be presented.

The various methods of producing pulmonary hypertension may be categorized as follows: (1) introduction of emboli into the lesser circulation, (2) creation of partial obstruction to pulmonary venous drainage, (3) exposure of the animal to various gas mixtures and/or altered atmospheric pressures, (4) systemic administration of drugs or foreign protein, and (5) increasing blood flow and/or pressure in the pulmonary arterial bed by the creation of systemic pulmonary shunts and/or reducing the pulmonary vascular bed.

REVIEW

Introduction of Emboli into the Lesser Circulation. Harrison [26] studied the lungs of patients who died with pulmonary hypertension and noted that the associated pulmonary vascular lesions superficially resembled arteriosclerosis but showed features suggesting that they might be the end stage of an organizing thrombus. He pointed out that Duguid [15] (1946) suggested that what is considered a typical coronary atheroma is, in fact, the end stage of an organizing thrombus. With this background Harrison [26] made intermittent intravenous injections of fragmented human blood clot in rabbits and sacrificed them at varying intervals. Significant lesions measuring 200 to 400 micra were found in the pulmonary arteries. The consistency of these ranged from that of recently impacted emboli to completely healed lesions depending on the time interval following cessation of the injections. The initial reaction appeared to be an infiltration of the entire vessel wall with polymorphonuclear leukocytes and macrophages frequently forming a cuff to surround the involved segment of vessel. Later the wall returned to normal with cell infiltration limited to the intima. Next, rapid replacement of clot with collagenous tissue and an increase of elastica

occurred in the form of a splitting off of the pre-existing layers to form new ones. There was a continuous process of consolidation over a period of about twenty-five days until there was a shrinkage of the intimal thickening and an increase in the luminal diameter.

Wartman [53] repeated Harrison's experiment except that he used autogenous clot for injections to rule out the possibility that an allergic response was the etiologic basis for the changes observed. The animals were followed for a longer period demonstrating essentially the same results as Harrison and showing further that the lesions healed following cessation of the injections and were not progressive.

Muirhead [41] utilized virtually the same technic and he injected a series of rabbits with human amniotic fluid in addition to blood clot. His results corroborated previous reports [26, 53] and suggested that the endothelial proliferation and necrotizing arteritis might be the result of impaired nutrition to the wall of the vessels distal to the lodged emboli.

Hepinstall [31] gave both normal rabbits and rabbits fed cholesterol intravenous injections of blood clot obtained from hypercholesterolemic rabbits. The normal animals had minimal cholesterol in the organizing emboli, while the diet group had a high proportion of the compound in their lesions.

There have been reports of the use of various foreign bodies such as lycopodium spores [8] and powdered graphite [5,6] to induce transient pulmonary hypertension in order to study the resulting acute changes in circulatory dynamics rather than the production of arterial lesions or permanent pulmonary hypertension.

Creating a Partial Obstruction to Pulmonary Venous Drainage. This category includes any procedure which either directly or indirectly raises the pressure in the pulmonary venous system. Hanlon [25] and associates demonstrated in dogs that the creation of a stenotic mitral valve 1 cm. or less in diameter caused an elevation in pulmonary venous pressure accompanied by a concomitant but lesser rise in pulmonary arterial pressure. Thus, there was a decrease in the pressure gradient across the vascular bed which reflected a decrease in resistance to flow. These investigators recently reported data about four dogs known to have had moderate to severe experimentally produced mitral stenosis for three to four years. While the pulmonary arterial pressures were not markedly elevated, the muscular pulmonary arteries demonstrated medial hypertrophy without intimal change. Barnes and associates [3] produced medial hypertrophy in small pulmonary arteries of the dog by wrapping the pulmonary veins with reactive cellophane.

Van Bogaert [52] has created pulmonary venous hypertension by anastomosing the left atrium to the side of the aorta. Medial hypertrophy of both the pulmonary veins and small muscular arteries appeared at four months in some animals.

Exposure of the Animal to Various Gas Mixtures and/or Altered Atmospheric Pressure. Campbell [6] (1922) reported hypertrophy of the muscular pulmonary arteries in rats exposed to low oxygen tensions in the environmental atmosphere for prolonged periods. Smith [50] and his associates subjected rats to 80 per cent oxygen mixtures for several months and noted that, after one month, the pulmonary arterioles were thickened with hyalinization of their walls and ultimate thrombosis of many. After forty-five days of exposure the larger pulmonary arteries demonstrated lesions of the media.

Valdiva [51] noted right ventricular hypertrophy in guinea pigs following subjection to atmospheric conditions equivalent to an elevation of 18,000 feet. Myocardial thickening which appeared after three weeks became conspicuous by two months. The pulmonary vascular bed appeared normal, and this was explained by the author as due to the relatively short period of observations.

Administration of Drugs or Foreign Protein. In 1950 Kawakami [32] narrowed the pulmonary arteries in castrated rabbits by daily injections of epinephrine for long periods of time. These changes consisted of both medial and intimal thickening. The effect of repeated injections of serotonin (5-hydroxytryptamine) on the pulmonary vasculature of experimental animals will be discussed in a subsequent section.

The administration of a foreign protein intravenously to a sensitized animal will usually provoke a general allergic response which varies in its manifestations from species to species [29]. Hawn and Janeway [29] administered bovine serum to rabbits not previously sensitized and produced a disease similar to serum sickness in man. A generalized arteritis which resembled periarteritis nodosa developed and was quite marked in the pulmonary vascular bed. No

mention was made as to whether pulmonary hypertension developed concomitantly. The arterial lesions were not progressive and demonstrated complete healing.

Increasing Blood Flow and/or Pressure in the Pulmonary Arterial Bed. An increase in blood flow and/or pressure to the lungs may be produced by one of two general methods: (1) The total pulmonary vascular bed may be reduced by removal of a portion of the lungs; or (2) a portion of the pulmonary arterial tree may be ligated leaving the corresponding lung tissue to be nourished by the bronchial arterial system. In the second method, an abnormal communication is created between the systemic and pulmonary circulations. Both of these methods have been used in the same animal by some investigators [*32,53*].

Adams [*1*] and associates noted that removal of the left lung caused a rise in pulmonary artery pressure from 32/5 to 44/5 mm. Hg which persisted for several months. In the same animal the pressure rose to 64/8 mm. Hg and death ensued when all of the right lung except for the upper lobe was removed. At postmortem examination, pulmonary edema of the remaining lung tissue was noted. Harrison [*27*] and associates demonstrated in dogs that reduction of the pulmonary vascular bed by 75 to 85 per cent by resection caused an immediate and sustained elevation in right ventricular pressure. They noted that the pulmonary arterial pressure gradually diminished over a period of five to six years so that it was only a few millimeters of mercury above preoperative levels. However, pulmonary arterial pressure increased by an average of 64 per cent with exercise in these animals.

Schilling [*49*] reported similar findings in dogs and described dilatation and hypertrophy of the right ventricle. He also described marked arterial hypertrophy associated with the compensatory emphysema and fibrosis that occurred in those animals which survived for considerable periods of time.

The second general method includes those experimental procedures which, by their design, produce an increase in pulmonary blood flow with or without an elevation in pressure to a part or to the entire lung. While interatrial and ventricular septal defects have been satisfactorily accomplished in the experimental animal [*28,33*], the development of associated vascular lesions or elevation of pulmonary pressure has not been reported. These procedures do increase pulmonary flow. If the defect was large enough and allowed to persist, it is conceivable that vascular lesions would develop.

Ventricular defects less than 1 cm. in size tend to close spontaneously while those that are larger produce congestive heart failure and subsequent death in the majority of animals [*33*]. Levy and Blalock [*35*] (1939) anastomosed the subclavian artery to the distal cut end of the left pulmonary artery in twelve dogs. Of the five that survived, none demonstrated any abnormality of the pulmonary vessels at the end of approximately six months. This particular approach to the problem was not reported again until 1953 when Muller, Dammann and Head [*43*] published their findings in a group of twenty-eight dogs subjected to one of three shunting procedures. In the largest group of animals (twenty-one) a shunt was constructed between the aorta and the distal cut end of the left pulmonary artery. The anastomoses were made as large as technically possible in view of Levy's and Blalock's [*35*] results. Five survived the procedure and lung biopsies at the end of one year demonstrated medial hypertrophy and some intimal hyperplasia of the small and medium muscular arteries in the involved lung. Pressures taken from within the pulmonary artery as far distal to the anastomosis as possible were noted to be only slightly less than those of the corresponding aorta. They reversed the flow of blood through the left upper lobe in three dogs and noted only minimal changes in the veins.

In subsequent reports, Dammann [*10,12*] and Baker [*2*] and their associates described the construction of an anastomosis between the pulmonary artery in the left upper lobe and either the subclavian artery or the side of the aorta in dogs. This procedure was not complicated by the development of cardiac failure, and the pressure on the pulmonary side of the shunt was consistently elevated to near aortic pressures. Serial biopsies obtained from the left upper lobe demonstrated that this procedure produced an acute arteritis followed by gradual healing with replacement of individual arteries by recanalized masses of connective tissue or a granulomatous type of endothelial lesion. Denervation of the left upper lobe did not affect the development of lesions. In a series of nineteen dogs subjected to this procedure, a left upper lobectomy was performed from one to

eleven weeks postoperatively. Repeated determinations of pressure were essentially the same as at the initial procedure. The initial reaction was dilatation and engorgement of all available vascular pathways. Next, the appearance of vascular and parenchymal injury was observed. Injury to the vessel wall was characterized by: (1) the presence of perivascular and intra-adventitial hemorrhage, (2) fragmentation of the elastica interna and externa, (3) actual rupture and necrosis of the vessel wall, and (4) an isolated and diffuse inflammatory response. Injury to the parenchyma was indicated by: (1) alveolar hemorrhage and edema, (2) interstitial edema, and (3) the later appearance of macrophages within the alveoli. These findings were thought to be the result of mechanical stress, that is, increasing the flow and pressure five times that normally borne by this lobe of the lung under normal function. As the acute phase subsided, the media and adventitia were noted to show an increase in fibrous connective tissue. Intimal proliferation was regarded as another manifestation of vascular injury. As the vessels progressively narrowed the lung parenchyma cleared as though the change in the vessels served to protect the remainder of the lung from the high pressure and flow.

Another interesting finding was that the vascular lesions seemed to spread gradually from the hilar area to the periphery of the involved lobe. It was postulated that this phenomenon might be the result of an increased extravascular pressure from hemorrhage and edema more proximally, thus effectively producing the actual intravascular pressure and protecting the vessels and parenchyma most distally. As healing occurred extravascular pressure would be reduced and intravascular pressure would be allowed to increase thus repeating the cycle of vascular injury on the more distally placed vessels.

Mature lesions appearing at eleven weeks were essentially similar to those produced by Harrison [*26*] by thromboembolism but, as the natural history of the former was so carefully followed, it seems highly improbable that the two are related.

Ferguson, Berkas and Varco [*21*] (1953) reported that the anastomosis of the subclavian artery to the distal end of the left pulmonary artery in dogs produced a rise in pressure in the latter to approximately 31 per cent of mean systemic pressure. The blood flow to the left lung in this series averaged 0.96 L. per minute as compared to 1.13 L. through the right lung. Removal of the left upper lobe in four dogs caused the pressure to rise from 38 to 60 mm. Hg. Constricting bands about the pulmonary veins of six dogs in this group caused no further increase in pressure. Microscopic study of lung sections taken from two weeks to eight and a half months postoperatively revealed medial hypertrophy of the pulmonary arterioles occurring as early as two weeks. Later, intimal proliferation associated with more severe medial hypertrophy of the same type of vessel was apparent.

Ferguson and Varco [*23*] extended these investigations (1955) and described various systemic-pulmonary shunts that they had constructed in a series of sixty-two puppies. They used the Fick principle to demonstrate a decrease in blood flow as well as increased resistance and elevation of pulmonary blood pressure in those lobes in which pulmonary arterial lesions developed. A gradual rise in pulmonary artery pressure also was noted upon opening the shunt and this was followed by a gradual fall in the majority of animals. This phenomenon was thought to represent active vasomotion in the pulmonary vascular bed, as there was no concomitant change in pulmonary venous or systemic pressure during the period of observation. There appeared to be more reaction in the pulmonary vessels when a systemic shunt is directed end to end into a branch of the pulmonary artery leading to the lung than when a similar shunt enters the main pulmonary artery, even though the amount of blood flow per unit of lung is as great or greater in the latter instance than in the former. They used special staining technics and believed that adequate demonstration was made to prove that the intimal proliferation was not due to elastic tissue degeneration or lipid infiltration.

Regression of pulmonary arterial lesions produced by various types of systemic-pulmonary shunts have been studied by Ferguson [*22,23*] and his associates. In six dogs in which systemic-pulmonary shunts had been constructed previously, the anastomosis was removed and the lobar pulmonary artery restored to its normal relationship with the patent pulmonary artery. Pulmonary artery pressures in all returned to normal. Four dogs which had demonstrated significant medial hypertrophy and intimal hyperplasia of the lungs at the initial procedure failed to show a definite evidence of

regression five to eight months following the reversal procedure. Biopsies were taken at intervals which equalled the time allowed for the lesions to develop. In one animal the reanastomosis had closed but the pulmonary artery was patent distally. The remaining animal demonstrated only medial hypertrophy at one month when the shunt was removed and was biopsied at the end of another month. The latter animal, which had only minimal changes at reversal, also failed to show any improvement of the vascular lesions. In the first four dogs described, a few vessels were noted which had intimal change with media which appeared to be relatively normal, an observation not made in lungs of animals when the shunt was functioning. There were occasional vessels in which the areas of intimal proliferation appeared to be recanalized. In no instance was there evidence that the vascular changes progressed following removal of the shunt.

The same authors [*22*] described the appearance of the pulmonary arterial lesions in three dogs at fourteen, twenty and twenty-one months after the shunt was reversed. All of these animals had demonstrated marked medial hypertrophy and intimal hyperplasia in the majority of small muscular arteries and arterioles in the involved area of the lung. These changes were interpreted as evidence that reestablishment of vascular patency occurs at a slow rate following removal of the provoking stimulus. The first definite change was the development of a more prominent capillary network within the proliferative intimal thickening. Some of these channels continued to enlarge until the original lumen appeared to be completely restored. Thickening of the media and adventitia appeared to become less pronounced, although there were some vessels in which there was no evidence of improvement. In many vessels, the cellularity of the intimal layer noted previously had decreased and a relatively larger proportion of collagen appeared.

METHODS

During the present investigation three different methods were used in an attempt to produce pulmonary hypertension and the associated pulmonary arterial changes.

Creation of Interventricular Septal Defects in Fetal Puppies. Since adult dogs do not tolerate ventricular septal defects of the magnitude associated with pulmonary hypertension in the human, it seemed worthwhile to attempt the procedure in fetal animals. The unique architecture of the fetal pulmonary vasculature might allow survival of animals having large septal defects at birth. The normally high pulmonary vascular resistance at this stage would tend to avert left ventricular failure which frustrates such attempts in the older dog.

A pregnant female dog was explored under nembutal anesthesia through a midline incision which gave adequate exposure of the bicornate uterus. The uterine wall was incised over a palpable fetus, and care was taken not to occlude the umbilical vessels. The amnion was left intact over the head to discourage spontaneous respiratory attempts. The chest was opened through the right fourth or fifth interspace and the pericardium incised anterior to the phrenic nerve. Initially, attempts were made to use a small cork borer to remove a portion of the septum. This method proved impractical because of the extreme friability of the myocardium. Other fetal animals were prepared in a similar manner and attempts were made to lacerate the septum with a cutting edged needle. This effort failed for the same reason as the previous one. The hearts seemed to be tolerant of considerable manipulation until excessive bleeding supervened. While these attempts were uniformly unsuccessful, the use of a fine insulated needle with only the tip exposed has been effective in selectively destroying the septum in autopsy experiments. It is hoped that this technic will prove useful in future experiments.

Administration of a Potent Pulmonary Arterial Vasoconstrictor to Newborn Rats. The report by Kawakami [*32*] that pulmonary arteriosclerosis was produced in rabbits following the prolonged administration of epinephrine suggested the possibility of producing a similar lesion by using serotonin (5-hydroxytryptamine). This compound which is normally present in the body has three to four times the vasoconstrictor effect on the pulmonary arterial bed as does epinephrine [*4,40*]. The effects of the repeated administration of serotonin on rats have been studied by various investigators [*14,39*]. While cutaneous and renal changes have been described, the pulmonary vessels have apparently been unaffected. A recent brief report by Rosi and Zamboni [*47*] describes the production of medial hypertrophy and intimal hyperplasia in medium-sized pulmonary arteries. MacDonald [*39*] observed that the

small pulmonary arteries of patients who had died with metastatic carcinoid tumors demonstrated slight but definite thickening of their walls. It was reasoned that, if the administration of the serotonin was begun shortly after birth, there might be a heightened response of the pulmonary vasoconstriction due to their thick-walled anatomic configuration at this stage; whereas, the pulmonary arteries in the adult are thin walled and not as mechanically efficient in constricting.

Standard albino rats were selected for this experiment because of their short gestational period. Four litters were given daily subcutaneous injections of serotonin beginning within twelve hours after birth. Doses selected were 2 mg./kg. for two litters and 4 and 10 mg./kg. for the remaining two litters. Serotonin precursor (5-hydroxytryptophan* was given in a similar manner to three additional litters in dosages of 5, 12.5 and 25 mg./kg. The injections were continued for ninety days in the group given serotonin and for sixty days in the animals treated with 5-hydroxytryptophan. Two litters were used as controls. One received daily subcutaneous injections of water in the same volume as used in the treated animals. The second group was not injected. Daily doses were regulated by weight changes and an attempt was made to avoid excessive volumes by preparing more concentrated solutions of the drug as the animals increased in size. The dosages were expressed as 5-hydroxytryptamine creatinine sulphate.

The animals were sacrificed at two weeks and one, two and three months. In addition several animals were allowed to survive two to three months following cessation of the injections. Initially, decapitation was used to effect sacrifice, but it was soon observed that pulmonary hemorrhage frequently resulted. Intraperitoneal nembutal was subsequently substituted.

Selected rats thirty days to five months old were anesthetized with intraperitoneal veterinary nembutal (4 cc./kg.) and placed in the supine position. The trachea was exposed and cannulated with a No. 15 needle which was utilized to administer intermittent positive pressure. Ventilation was provided at a set pressure and flow for all animals. The heart was exposed and pressures were measured in the right ventricle by inserting a No. 20 needle connected by a tube filled with saline to a transducer which was coupled with an electronic recording device. In seventeen treated animals, the right ventricular systolic pressure varied from 9 to 43 mm. Hg with an average of 13.8. Four control animals had systolic pressures ranging from 5 to 14 mm. Hg with an average of 8 mm. Hg.

The heart and lungs of each animal were removed and allowed to fix in formalin for at least two weeks. Duplicate sections were then prepared and stained with both hematoxylin and eosin and Verhoef-Von Gieson connective tissue stains. The pulmonary arteries and arterioles were then inspected to ascertain any differences between the control and treated animals. While animals were sacrificed at varying intervals throughout the experiment, the specimens which were obtained at intervals of one, two and three months received the most attention. Medial thickening of the small muscular arteries and arterioles was present in each of the specimens studied but no consistent pattern of changes could be found that differed significantly from those of the control animals obtained at a similar period. In fact, some of the control animals had arterial changes that were more marked than any of those observed in the treated group. Determination of lumen to wall ratios in selected specimens confirmed the failure of the treated animals to show significant arterial narrowing. Those animals allowed to survive several months after interruption of the injections did not show progressive arterial change.

The limited number of animals in which pressure data was obtained does not allow any conclusions to be made regarding the production of pulmonary hypertension. In this experiment it was apparent that the elevation of right ventricular pressure was not a consistent finding. The histologic changes were very misleading when viewed separately in that they appeared typical of a high resistance pulmonary vasculature, but the control sections revealed an almost identical configuration. The normal regression of the thick-walled fetal pulmonary arterial system may require longer than the time allowed in this study. A thorough study of the evolution of the pulmonary arterial sys-

* 5-hydroxythyptophan was kindly furnished by A. O. Goiszler of Abbott Laboratories Research Division, North Chicago, Illinois. 5-hydroxythyptamil was furnished by Merrill E. Speeter, Head, Department of Biochemistry, The Upjohn Company, Research Division, Kalamazoo, Michigan.

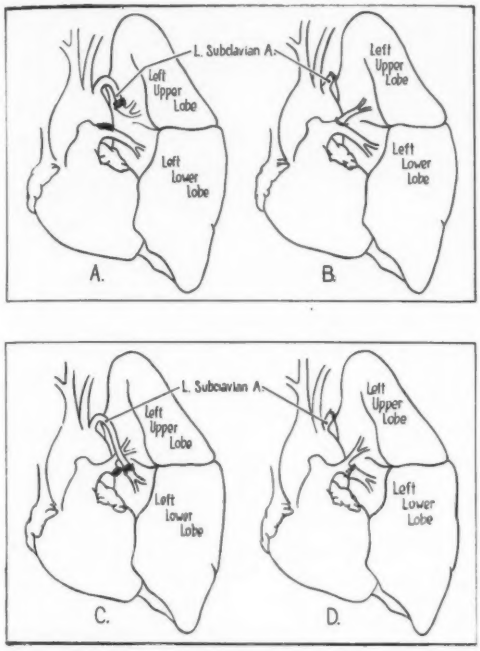


FIG. 1. Subclavian-left upper lobe pulmonary arterial anastomosis (A) and reversal (B) are shown at the top. Subclavian-left lower lobe pulmonary arterial anastomosis (C) and reversal (D) are shown at the bottom.

tem in the rat is necessary in order to carry out a similar experiment.

Construction and Subsequent Reversal of Systemic-Pulmonary Lobar Artificial Shunts in Dogs. The sequence of development of pulmonary arterial lesions in the upper lobe of the dog lung exposed to a systemic blood pressure and flow was outlined in the preceeding review. The present experiment is concerned with the changes in similarly produced lesions following interruption of the inciting hypertensive stimulus. Our major interest centered around changes that were similar to the "high resistance-low reserve" pattern described by Edwards [*19*]. Initially, our intention was to determine whether or not a stage in the development of the lesions could be determined beyond which regression could not occur. As the experiment progressed it became evident that even the most advanced lesions produced by this technic demonstrated indication of healing upon removal of the systemic shunt.

An end to end anastomosis between the subclavian artery and the pulmonary artery in the distal left upper lobe was constructed in forty-six adult mongrel dogs. (Fig. 1A.) In fourteen other animals the pulmonary artery in the distal left lower lobe was anastomosed to the side of the aorta or to the end of the subclavian artery. (Fig. 1C.) At intervals varying from one hour to nine months, the anastomosis was interrupted and the lobar pulmonic artery was reanastomosed to the left pulmonary artery in twenty dogs. (Figs. 1B and C.) Arterial pressures were recorded in the aorta, subclavian and involved pulmonary artery at both procedures in the majority of animals. The involved lung was biopsied or removed at periods of a few hours to one year after the "reversal" operation. Microscopic sections were prepared with both elastic tissue and hematoxylin and eosin stains and multiple sectioning technics were used in those animals severely affected in order to avoid misinterpretation of focal changes.

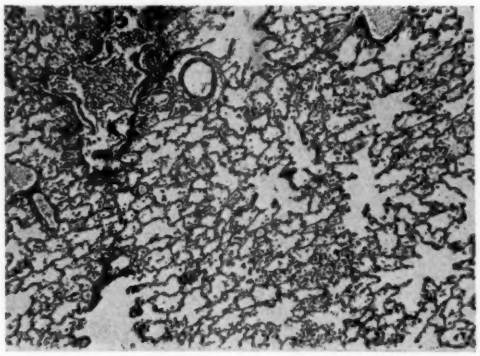


FIG. 2. Biopsy of the lung in the control animal demonstrating normal thin-walled, muscular arteries and arterioles.

A comparison was then made between control sections (Fig. 2), biopsies obtained at the reversal operation, and the final specimens obtained in each animal at sacrifice or autopsy. Objective evidence of healing which occurred between the reversal operation and the time of the final biopsy was determined by several methods. Changes in the walls and lumens of the pulmonary arteries in the various sections of each animal having advanced lesions were measured with a micrometer eye piece, and the lumen to wall ratios were calculated. The difference in the total number of obstructed arteries per lower power field in the prereversal and postreversal sections was also used as an index of regression.

FIG. 3. Cast of pulmonary artery of the left lower lobe which had been subjected to systemic blood pressure and flow for eighteen months. Cast of pulmonary arteries from normal subject is shown for contrast (right).

Forty per cent of the animals succumbed in the early postoperative period. The majority of deaths were attributed to pulmonary edema. The anastomosis was found to be thrombosed in six animals at the time that the second biopsy was obtained. At the operation for final biopsy, the reanastomotic suture line was found to be patent in four animals and thrombosed in seven, but was not examined in two animals. In the animals with thrombosis of the reversal anastomosis, the distal lobar pulmonary artery was found to be patent in each case, as shown either by angiogram or actual dissection of the artery for several centimeters into the parenchyma of the lung and subsequent inspection.

COMMENTS

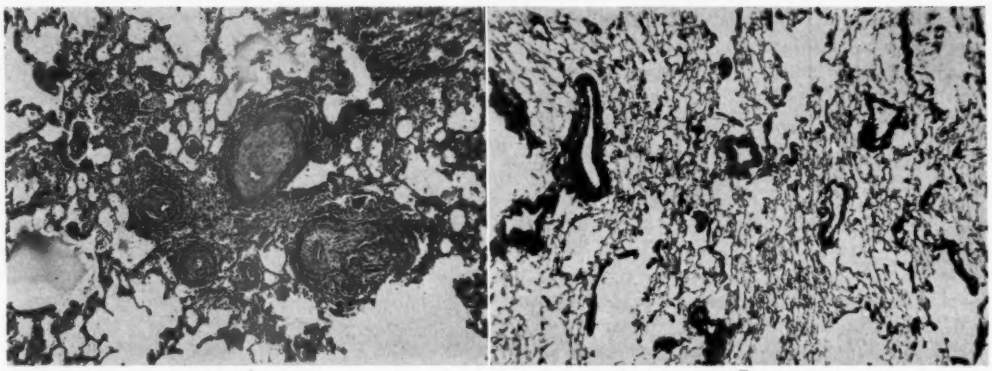
The development of the arterial changes was similar to the sequence described previously. It was observed that anastomosis of the subclavian artery to the left upper lobe pulmonary artery produced the most consistent vascular lesions. Those animals having the lower lobe pulmonary artery anastomosed to a systemic vessel did not develop advanced lesions within six months. One dog that had the left lower lobe pulmonary artery anastomosed end to side to the aorta was allowed to survive eighteen months before the second operation. The pressure in the distal pulmonary artery of the involved lobe equalled that in the aorta at the reversal procedure. Death occurred during the first postoperative day from atelectasis of the right lung. Injection of the affected lobe with a radiopaque contrast medium revealed uniform blockage of the smaller pulmonary arteries. (Fig. 3.) The anatomic changes consisted of marked medial hypertrophy and intimal hyperplasia of the medium and small pulmonary arteries.

The arterial pressures on the pulmonary side of the anastomosis generally correlated with the vascular alterations which subsequently developed. If the pulmonary artery pressure did not approximate systemic levels, the vascular changes were usually minimal. There was frequently increase in the lobar pulmonary artery pressure between the first and second operations which was interpreted as representing an increased resistance to blood flow through the involved lobe.

In two animals in which the systemic-pulmonary artery shunt was interrupted at the end of one hour and one week, respectively, the hemorrhagic pneumonitis and perivasculitis demonstrated significant clearing by the end of three months. Increased perivascular adventitial tissue was noticeable about the small muscular arteries and arterioles at the end of this time, however, but the luminal diameters did not appear to be reduced.

In five animals in which reversal after longer intervals was performed, minimal to moderate degrees of hypertrophy of the medial layers of the muscular arteries and arterioles occurred. The degree of healing occurring between the second and third operations in this group was difficult to assess. The thickness of the wall of the involved arteries appeared to be reduced in most instances although perivascular fibrosis was usually present in the final sections. Progression of the vascular lesions was not observed following interruption of the hypertensive stimulus.

Six animals had developed advanced pulmonary arterial lesions consisting of varying degrees of both medial hypertrophy and intimal hyperplasia. (Fig. 4A.) Examination of microscopic sections obtained from several hours to four months following the reversal operation revealed noticeable increase in luminal diameters of the involved vessels as early as eleven days postoperatively. While the majority of vessels still bore evidence of injury as reflected



4A 4B

FIG. 4. A, peripheral lung biopsy obtained at the reversal operation four months following establishment of a subclavian-left upper lobe pulmonary arterial anastomosis. Notice the degree of luminal occlusion caused by proliferative intimal changes in the pulmonary arteries. B, biopsy obtained from the same area of involved lung three months after the reversal operation. While evidence of vascular injury is still present, the over-all cross-sectional diameter of the pulmonary arteries is significantly increased. Original magnification, × 70.

by the fragmented elastic lamina and intimal fibrosis (Fig. 4B), there appeared to be a significant increase in the over-all cross-sectional diameter of available vascular pathways. This was confirmed by the lumen to wall ratio determinations and objective counting of the number of totally obliterated arteries in the prereversal and postreversal biopsy material.

Since we realized that functional studies are of importance in such a study, an angiogram of the pulmonary vascular bed at the second operation was obtained and correlated with another obtained later during the healing period. The initial results with this technic support the impressions gained by histologic study alone.

The consistent production of advanced pulmonary arterial lesions can most readily be achieved by subjecting the upper lobe of the dog lung to a systemic blood flow and pressure. Using larger areas of lung required a much longer period of time to produce comparable lesions.

The role of trauma in the etiology of the observed changes deserves comment. Undoubtedly the acute changes produced in this experiment are not analogous to the early changes in the lungs of patients with congenital heart disease, but the end result is similar. Stages in the development of the lesions are identical in that medial hypertrophy of the smaller muscular arteries and arterioles is followed by the appearance of intimal hyperplasia. The degree of fibroplasia and actual replacement of elastic tissue with mature fibrous tissue is probably the deciding factor. Thus, reversibility would be enhanced if nuclear activity in intimal proliferative lesions is high. In contrast, a more permanent lesion is probably present if mature fibrous tissue having only sparse nuclei fills the vessel lumens.

The apparent early attempts at healing in even the most severely affected pulmonary vascular beds in this study is encouraging. However, the question arises as to whether or not a similarly involved vasculature will have the capacity to increase its functional lumen size in the presence of higher blood flows and pressures than were produced in this experiment. This will be the case clinically since closure of an intercirculatory communication places an equal or greater burden on the lesser circulation so affected. It is for this reason that we are presently seeking other experimental preparations that more closely resemble the functional and anatomic changes as they occur in man.

SUMMARY

A brief review of previously described methods of producing experimental pulmonary hypertension has been presented.

Three technics that we have used in attempting to induce pulmonary arterial disease are described. These technics were: (1) creation of interventricular septal defects in fetal puppies, (2) the administration of serotonin to newborn

rats, and (3) systemic-lobar-pulmonary arterial anastomoses in dogs. The systemic-lobar-pulmonary arterial anastomoses proved to be the most satisfactory technic and produced pulmonary arterial lesions similar to those seen in man in the majority of survivors in this group of animals. The reversibility of these changes was determined by histologic study of the lung following anastomotic restoration of the pulmonary artery to the involved lobe. Those animals showing both medial hypertrophy and intimal hyperplasia demonstrated a significant increase in the cross-sectional area of the pulmonary arteries following the reversal operation. Medial hypertrophy alone or with minimal intimal sclerosis appeared to regress at a slower rate but in no instance did a progression of the observed changes occur.

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Pancreatic Secretion and Peptic Ulcer Formation

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MANN and Williamson [3] (1923) established the fact that pancreatic juice diverted from the duodenum, either to the outside or into the lower bowel, leads to formation of duodenal ulcer.

Dragstedt [2] (1943) revealed the development of ulcers in almost 100 per cent of experimental dogs with total external pancreatic fistulas.

Poth [4] (1948) suggested that the pancreas may have an intrinsic influence upon the formation of ulcers other than mere neutralization of the gastric acid chyme in the duodenum. This investigator produced fulminating peptic ulcerations by the action of histamine following pancreatectomy or ligation of the pancreatic ducts. It was further suggested that perhaps both "the internal and external secretions of the pancreas may be implicated in ulcer formation."

These suppositions were climaxed by the initial report of Zollinger and Ellison [6] in 1955 of two cases of fulminating ulceration of the upper jejunum associated with a nonspecific islet cell tumor (non-beta cell adenoma) of the pancreas. Since this initial report, approximately 80 similar cases of ulcerogenic tumors of the islet cells in the pancreas have been recorded.

This report covers the history of three patients who were treated at the University of Texas Medical Branch Hospitals. All of them were women; one was white and two were Negro.

CASE REPORTS

CASE I. C. R., a thirty-four year old white woman, had had symptoms of peptic ulcer since January 1945. There had been five episodes of hematemesis between June 1945 and March 1946.

On April 11, 1946 a partial gastrectomy was performed. One-third of the stomach was resected. A mass was palpable in the head of the pancreas. This mass was considered to be the site of a posterior ulcer perforating into the pancreas.

On June 25, 1946 the patient was operated upon for a perforated stomal ulcer. A stormy febrile postoperative course followed. The patient returned to her home, continued to do poorly and died on September 10, 1947. Autopsy revealed: adenocarcinoma (grade II) of pancreas with metastasis to the liver, chronic pancreatitis, healed duodenal ulcer, superficial ulceration of the duodenum, and lower nephron nephrosis of Lucke.

The tissue slides were obtained in 1958 and studied by Dr. John Childers, Pathologist at this Institution. A diagnosis of islet cell carcinoma was made.

CASE II. A. T., a thirty-three year old Negro woman, had a history of ulcers since 1953. Roentgenographic diagnosis of two active duodenal ulcers was made on March 3, 1953. Unrelenting ulcer disease required several hospital admissions culminating in an added diagnosis of hyperparathyroidism.

April 28, 1958 two parathyroid adenomas were removed with relief of the hyperparathyroidism.

A twelve-hour, overnight, interdigestive gastric analysis on October 7, 1958 revealed a volume of 2,200 cc. with 164 mEq. of free acid and 186 mEq. of total acid.

On October 10, 1958 a partial gastrectomy was performed. Two-thirds of the stomach was resected. Two benign islet cell adenomas of the pancreas were excised locally.

Skull films on November 13, 1958 were reported as normal. Determination of 17-ketosteroid and 17-hydroxysteroid levels in the urine was done on December 20, 1958 (17-KS* levels were 7.32 mg./24 hr., 17-OH† levels were 11.40 mg./24 hr.). A second determination on December 21 revealed that 17-KS levels were 5.86 mg./24 hr. and 17-OH levels were 10.74 mg./24 hr.) Both were within normal limits.

* 17-ketosteroid; † 17-hydroxysteroid.

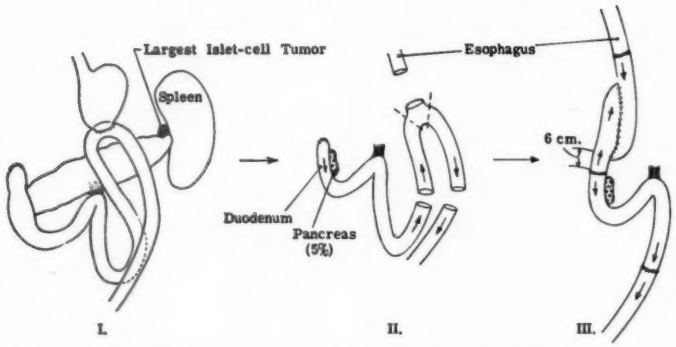

FIG. 1. A schematic representation of the final operative procedure performed on Case 11 on December 3, 1959. I, remnant of stomach, the excluded duodenum, the intact pancreas and spleen with location of largest islet cell tumor are shown. II, extent of resections is shown. Duodenum has been opened, explored and two islet cell tumors excised from duodenal wall, 95 per cent of pancreas containing twelve islet cell tumors resected, splenectomy, resection of the gastric remnant and preparation of jejunum for reconstruction. III, shows construction of substitution gastric pouch and re-establishment of esophagoenteric continuity.

The peptic ulcer disease recurred within one month. The patient was hospitalized again on March 4, 1959 because of continuing ulcer symptoms. A twelve-hour interdigestive gastric analysis was done with Pamine® 0.25 mg. given intramuscularly every four hours during the latter half of the analysis. The volume was reduced by the Pamine from 850 cc. to 202 cc., the free acid from 29.98 mEq. to 3.02 mEq., and the total acid from 47.52 mEq. to 8.80 mEq. These values are corrected to cover a period of twelve hours. This inhibition of gastric secretion by a parasympatholytic drug is contrary to the usually accepted concept that vagal blockade has no influence on the rate and character of gastric secretion stimulated by an ulcerogenic islet cell tumor of the pancreas.

Roentgenograms of the skull on March 13, 1959 revealed an enlarged sella turcica. The radiologist reported that findings were consistent with the presence of a lesion of the pituitary. Urinary levels of 17-ketosteroid and 17-hydroxysteroid were again determined on March 14 (17-KS levels were 15.34 mg./24 hr. and 17-OH levels were 12.98 mg./24 hr.) These levels were in the upper limits of normal.

In May 1959 two blood transfusions were required because of hematemesis.

The patient was readmitted to this hospital on October 13, 1959. X-ray examination on October 14, 1959 revealed multiple marginal ulcers. Her condition grew progressively worse. Several attempts were made to do interdigestive, twelve-hour gastric analyses. Now, in contrast to high volume flows and high acidity, the secretions were so tenacious and thick that they could not be aspirated. An acceptable analysis could not be made. While the analysis was unsatisfactory, it is well to record the results of twelve-hour interdigestive secretions. The volume was 402 cc. There was no free acid and the total acid was 3.80 mEq. Intramuscular Pamine (0.25 mg. every four hours) altered the gastric secretion. The volume was 90 cc. no free acid and total acid 1.12 mEq. Obviously, the free acid could not be lowered, but the total acid was decreased. These values in themselves are not important, but neither is it clear why this patient continued to have severe peptic ulceration and symptoms at a time when no free acid could be recovered. Multiple islet cell tumors were present in the duodenal wall and throughout the pancreas.

Urinary levels of 17-ketosteroid and 17-hydroxysteroid were again determined on October 27, 1959 (17-KS levels were 11.41 mg./24 hr., 17-OH levels were 16.93 mg./24 hr.). On October 28 levels were as follows: (17-KS, 13.47 mg./24 hr.; 17-OH, 16.28 mg./24 hr.). The 17-ketosteroid levels were within normal limits, and the 17-hydroxysteroid levels were only slightly elevated. Roentgenograms of the skull taken on November 30, 1959 showed that the diameter of the sella turcica was within normal limits. Bilaterally, the visual fields were somewhat constricted. There were no reductions in the temporal fields. The absence of headache and other evidence of increased intracranial pressure or progressive enlargement of the sella, resulted in the conclusion that the pituitary gland was not involved.

On December 3 a second exploratory laparotomy was performed and the following was accomplished:

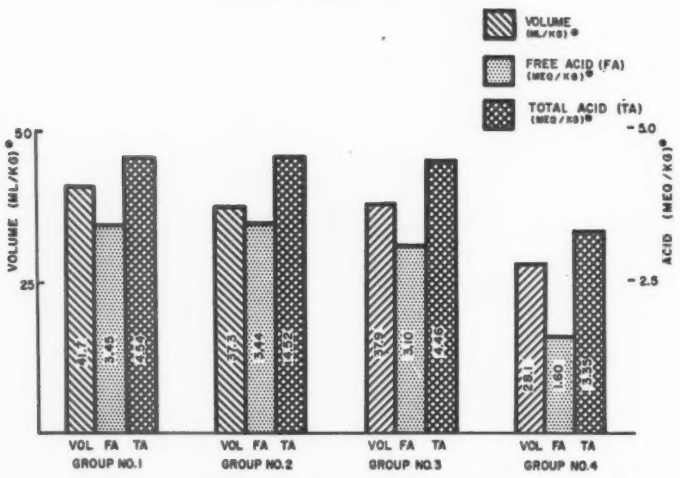

FIG. 2. The results of the subcutaneous injection of tissue extracts into Shay rat preparations. Four groups of experiments as follows: Group I, eight animals, average weight 99 gm., controls, no injections. Group II, eight animals, average weight 98.1 gm., injection of saline extract of normal dog pancreas. Group III, six animals, average weight 111.1 gm., injection of saline extract of pancreatic tumor tissue from patient. Group IV, six animals, average weight 104.3 gm., injection of saline extract of pancreatic tissue from patient which contained no gross tumor. Attention is directed to the observation that the gastric secretory activity of the control animals (Group I), those animals receiving injections of saline extracts of normal dog pancreas (Group II), as well as the animals which received injections of saline extracts of the islet cell tumor tissue (Group III) showed essentially identical responses. The only alterations observed follow the injection of saline extracts of the patient's pancreatic tissue which is grossly free of tumor tissue. The activity seen is one of suppression of free acid to about half and the total acid to approximately three-fourths; that is, a suppression of total acid secretion without an increase of the buffering substances in the stomach. These data, volume in milliliters and acid in milliequivalents, are expressed as these quantities per kilo of body weight of the experimental animals.

(Fig. 1) (1) subtotal pancreatectomy (5 per cent of the head was preserved), (2) duodenostomy with local excision of two islet cell tumors, (3) resection of gastric remnant, (4) splenectomy, (5) construction of the gastric pouch from the jejunum with reversed peristaltic outlet according to the technic described by Poth [5]. (6) esophagojejunostomy (to the pouch), (7) jejunoduodenostomy (reversed peristaltic pouch to duodenum), and (8) jejunojejunostomy.

Twelve benign islet cell tumors were found in the pancreas and two benign islet cell tumors were excised from the wall of the first portion of the duodenum. These adenomas showed considerable pleomorphism in some areas but this was not thought to constitute sufficient evidence that malignant transformation had occurred. These benign neoplasms were considered to be of multicentric origin.

Convalescence was uneventful. At present the patient is able to eat a full diet with supplementary pancreatic extract. There is no dumping or diarrhea. The patient has gained weight. B_{12} absorption studies reveal a deficiency of the intrinsic factor. Studies of fat and protein absorption show them to be normal.

CASE III. P. W., a thirty-one year old Negro woman, gave a history of illness of one year's duration, which was characterized by nausea, vomiting and watery diarrhea.

X-ray examination on June 9, 1959 revealed a scarred duodenal cap and an abnormal small bowel pattern which was diagnosed as obstruction. A single gastric aspiration on June 16, 1959 revealed 42 clinical units of free acid and 48 clinical units of total acid. Stools were positive for occult blood and the hemoglobin fell rapidly from an admission value of 11.8 to 7.9 gm. per cent.

On July 10, 1959 an abdominal roentgenogram revealed free air under the diaphragm. A large, perforated anterior duodenal ulcer was closed at oper-

ation. The remainder of the small bowel appeared normal.

Postoperatively, a large amount of secretions (averaging 1,500 to 2,000 cc. per day) drained from the gastric tube. The patient died suddenly on July 20. The immediate cause of death was not apparent on autopsy. Parathyroid, pituitary, and adrenal glands were normal, and the duodenum contained no tumors. The pancreas was grossly normal, but on serial section a small tumor (4 to 5 mm. in diameter) was found in the lower edge of the pancreas. Microscopic study revealed carcinoma of the islet cells. No metastases was found.

SPECIAL STUDIES

Saline extracts of fresh islet cell tumor tissue from A. T. (Case 11) were studied in an attempt to determine specific, direct, physiologic activity.

A modification of the Shay rat preparation was employed for some of these studies. The animals were starved for twenty-four hours and allowed water *ad lib.* until the time of weighing. The animals were weighed, marked and separated into four groups as set forth in Figure 2.

Animals were anesthetized with ether. The operative procedure consisted of tying a moderately loose loop around the pylorus thereby creating an artificially induced pylorospasm, and the abdomen was closed. Injections of the tissue extracts were given subcutaneously at the conclusion of the operation. The animals were allowed to recover from the anesthetic and then sacrificed after three hours by the administration of an overdose of ether. The esophagus was clamped and the stomach with its contents recovered.

The contents were measured to the nearest 0.1 ml., diluted to bring the total volume to 20 ml. and titrated against N/10-NaOH to the end points of Topfer's reagent and phenolphthalein indicators. The volume of gastric juice secreted (in milliliters) and the acid (in milliequivalents) were calculated as quantities per kilogram of body weight as given in Figure 1.

Mongrel dogs anesthetized with intravenous barbiturates were prepared as acute experiments to record blood pressure, pulse rate and magnitude of respiration. The intravenous administration of acetic acid extracts of the tumor tissue had no demonstrable pressor or depressor effects.

These studies failed to reveal any specific, physiologic activity of fresh extracts of the tumor tissue.

COMMENTS

The original report of Zollinger and Ellison [6] described the coexistence of islet cell tumors of the pancreas and fulminating peptic ulcers and postulated an ulcerogenic humoral factor arising from these pancreatic islet cell adenomas.

Ellison [1] (1956) reported documented observations of the return of gastric secretions to normal levels following ablation of an islet cell tumor of the pancreas which did not produce insulin. He suggested that a hormonal or chemical factor arising in the pancreatic tumor was capable of stimulating the gastric glands to secrete.

Zollinger [7] (1958) again suggested that ulcerogenic tumors of the pancreas had a direct influence on gastric secretion.

Tumor tissue from A. T., Case 11, was studied in an attempt to demonstrate direct physiologic activity in fresh extracts of this tissue using the Shay rat and the dog. None was found.

It appears probable that the observed increase in gastric acid secretion is likely due to an indirect mechanism. Studies have been initiated to discover such a relationship. It is postulated that the parietal cells of the gastric glands have the inate property of continuous, maximum secretion. The species man and dog have a balancing, inhibitory mechanism to keep the rate of secretion in check. The intestinal phase of gastric secretion is such an inhibiting mechanism. This inhibiting mechanism is apparently absent in the rat resulting in the gastric secretory rate being continuously near maximum in this species.

Certain aspects of the various experiments of Mann and Williamson support the thesis that the relation between pancreatic endocrine and/or exocrine secretions influence parietal cell activity by an indirect rather than by a direct mechanism. The observations of Poth [4] that the dog develops fulminating peptic ulceration following the administration of histamine when the exocrine secretions of the pancreas are excluded from the duodenum may be further support of an indirect mechanism by which islet cell tumors of the pancreas are ulcerogenic.

The failure to find substances in the extracts of fresh islet cell tumor tissue may mean that the action is an indirect one rather than a direct stimulation of parietal cell activity. While it is always possible, it seems unlikely that the

active substance was lost during these simple direct studies.

Blockade of vagal impulses by a parasympatholytic drug reduced the rate of acid secretions of the parietal cells in a proved case of ulcerogenic tumor of the pancreas. This observation is contrary to that usually held.

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Late Results of Hiatus Hernia Repair

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A STUDY of the late results of hiatus hernia repair was undertaken primarily because of our interest in the mechanism and correction of secondary anemia due to blood loss associated with hiatus hernia. However, an important result of this study is confirmation of our growing belief that the long-term results of hiatal hernioplasty as measured by recurrence rate and relief of subjective symptoms leave much to be desired. Our experience indicates that the early evaluation of the results of hiatus hernia repair discloses only a small number of the patients destined for eventual recurrence of herniation and/or symptoms. The study indicates that hiatal hernioplasty is quite efficacious in relieving associated bleeding and the anginal type of pain. It is less likely to afford relief of other symptoms such as dysphagia, regurgitation and dyspepsia. Further, satisfactory results are most difficult to attain if there is esophageal foreshortening to an extent precluding repair of the herniation by ordinary means.

GENERAL CONSIDERATIONS

This study concerns hiatus hernia patients treated surgically at the University and Veterans Administration Hospitals in Iowa City from 1947 to 1957. Nine of the total of 109 patients were omitted because their hernias were small and asymptomatic and the repairs were incidental to other major abdominal procedures such as gastric resection, cholecystectomy and colon resection. There were two operative deaths following transthoracic hernioplasty. One was due to pneumonia and the other was attributed to pulmonary embolism. In seventy-eight of the remaining ninety-eight patients late clinical evaluation was possible for two to twelve years following operation (average more than five years) by means of re-examination [*17*] as outpatients or by correspondence [*61*] with the patients or the patients and their family physicians. Thirty-eight of these seventy-eight patients were males, and the age range was eighteen to seventy-seven, averaging fifty-nine years.

Accurate classification of the hernias as sliding or para-esophageal types proved to be impossible. However, most of the hernias were of the pulsion or sliding variety. Only a few were of unquestioned para-esophageal type with the cardia in a normal location below the hiatus.

It was found advantageous to categorize the patients according to their dominant initial symptoms or findings into the following groups: dyspepsia, bleeding, esophageal dysfunction, and pain of anginal type. Table 1 indicates the frequency of these categories in the patients in whom late results were determined.

The greatest number of patients (thirty-nine or 50 per cent) were classified as dyspeptic because of the nondescript nature of their symptoms such as nausea, vomiting, epigastric discomfort, "sour stomach," vague cramps, fullness and belching, and specific food intolerance. Barium studies did not reveal duodenal or gastric ulcer in any of these patients. Unfortunately, esophagoscopy and cholecystography

TABLE 1
INDICATIONS FOR REPAIR (78 PATIENTS)

Symptom	No. of Patients
Dyspepsia	39
Bleeding (4 acute, 14 chronic)	18
Esophageal dysfunction	16
Pain (anginal-type, radiating)	5
Total	78

TABLE II
HIATUS HERNIA WITH SHORTENED ESOPHAGUS*

Patient	Date of Operation	Symptom	Procedure	Results
A. W.	6–19–47	Dyspepsia	Hiatal enlargement	Well 12 yrs, then hematemesis from esophageal ulcer
R. B.	2–25–50	Dysphagia and regurgitation	Esophago-gastric resection	Anastomotic stricture at 4 mos. required re-resection
F. B.	3–17–50	Dyspepsia	Esophageal advancement	No follow-up information
P. H.	10–2–52	Dysphagia	Hiatal enlargement	Well for 7 years
C. W.	6–2–54	Dysphagia	Hiatal enlargement	Died 2 days postoperatively of pulmonary embolism
C. O.	2–29–56	Pain and regurgitation	Hiatal enlargement, angle His re-established	Well for 2 years
C. H.	6–28–56	Regurgitation	Esophageal advancement	Recurrent hernia and hematemesis at 8 mos., reoperated upon, died 18 days postoperatively of pneumonia

* The only two postoperative deaths in the series of 100 symptomatic patients occurred in this group.

was not invariably performed although it was usually done preoperatively. However, none of these studies revealed esophagitis or cholelithiasis. Barium enema studies of the colon were seldom obtained in this group.

Bleeding was second in frequency (eighteen or 24 per cent) as an indication for operation. It was acute in four patients and chronic in fourteen. The most common cause of the blood loss was diffuse esophagitis or esopahgeal ulcer. In one patient the acute bleeding was from a gastric ulcer located within the herniated stomach. Several patients lacked evidence of esophagitis or ulceration and were assumed to be losing blood from the mucosa of herniated stomach, the external wall of stomach appearing congested [9]. Biopsy of herniated gastric wall in three such cases revealed edema and congestion grossly and congestion of mucosa and hemorrhage into mucosa, submucosa and the lumina of gastric glands microscopically. It seems that "hemorrhagic gastritis" of the herniated stomach without gross gastric ulcer, as well as esophagitis without gross esophageal ulcer, may be the source of chronic blood loss in patients with hiatus hernia.

Symptoms of esophageal dysfunction (regurgitation, dysphagia, "sticking") were next in frequency (sixteen or 20 per cent). In four of these patients esophagitis had led to severe shortening of the esophagus so that unusual operative technics were employed. (Table II.) Distinct esophageal ulcer was found in one patient. One patient (R. H.) had an active duodenal ulcer in association with the hernia. This patient was treated by transabdominal hernioplasty and vagotomy with partial gastrectomy. In three other patients of this group cholelithiasis coexisted and cholecystectomy was performed at the time of hernia repair. The frequency of related abdominal lesions in these patients (four of the sixteen) emphasizes the importance of careful preoperative evaluation of the biliary and gastrointestinal tracts in patients with symptomatic hiatus hernias and suggests the adoption of abdominal repair whenever reasonable so that abdominal exploration may be thorough.

The least common complaint leading to hiatal hernioplasty (five patients) was lancinating pain in the anterior chest or epigastric region with radiation to the shoulder in two patients. As the pain was anginal in character, these patients were evaluated carefully prior to operation for evidence of cardiac disease by clinical and electrocardiographic means.

TECHNICS AND RESULTS

No unanimity of opinion existed among the thirty-four staff and resident surgeons as to the proper method of exposure and repair of hiatus hernias. So many technics were utilized by numerous surgeons that no valid conclusions could be drawn as to the efficacy of the various approaches or methods of repair. Repairs performed by the thoracic surgical section were ex-

clusively through the chest and intra-abdominal lesions were not treated at the same operation in any of the patients. Those classified as general surgeons used several approaches to the hernias and often undertook correction of other abdominal lesions which were variously considered related or coincidental (such as duodenal ulcer, cholelithiasis, and elevated gastric acid secretion). Generally, in instances in which esophageal length was not a problem, the hernia was reduced and the esophagus was left in the hiatus. The hiatus was then narrowed by crural approximation behind the esophagus [*1*] or by crural reefing to the left of the esophagus [*6*]. Occasionally a surgeon tended to advance the esophagus foreward from the hiatus toward the dome of the diaphragm fairly routinely. Certain adjunctive technics occasionally employed included suture of the esophagus to the hiatus, suture of the stomach to the inferior surface of the diaphragm, suture of peritoneum and/or phrenoesophageal ligament to the under surface of the diaphragm and lateral suture of lower esophagus and upper stomach to re-establish the angle of His [*8,10*]. Occasionally, during transthoracic repair an incision was made in the diaphragm away from the hiatus to facilitate hernial reduction or subdiaphragmatic fixation of the phrenoesophageal ligament, peritoneum or stomach. Less commonly a diaphragmatic incision was made primarily to permit limited exploration of the upper abdomen.

Shortened esophagus (apparently of secondary rather than congenital origin) of a degree sufficient to demand extraordinary technical management was encountered in seven patients. (Table II.) Transthoracic exposure was utilized in all seven patients. In one patient (R. B.) who had esophagitis and esophageal ulcer, esophagogastric resection and intrathoracic esophagogastric anastomosis was performed. Re-resection was necessary five months later for relief of anastomotic ulcer and stricture. We could obtain no information about his subsequent course. In two patients (F. B., C. H.) with shortened esophagi, esophageal advancement enabled replacement of cardia to an infradiaphragmatic location. No information could be obtained about one (F. B.) of these two patients. The other (C. H.) patient returned eight months after operation with recurrent hernia (demonstrated by roentgenogram) and esophageal bleeding. At re-operation, esophageal shortening had progressed to the extent that the cardia could not be placed in an infradiaphragmatic location despite phrenic nerve crush. Therefore, the esophageal hiatus was enlarged to provide an opening three to four inches in diameter and the margins of the diaphragm were sutured to the stomach in its midportion, deliberately placing half of the stomach in the chest [*5*]. Vagotomy and pyloroplasty were added. This patient died of pneumonia eighteen days following operation. In the other four patients with shortened esophagi no attempt was made to replace the stomach infradiaphragmatically because of the degree of esophageal contraction. In all four, the hiatus was enlarged and the margins were sutured to stomach as previously described [*5*]. In one of these (O. O.) the fundus of the stomach was sutured to the esophagus to re-establish the angle of His intrathoracically as advocated by Watkins [*10*]. One of these four patients (C. W.) died two days after operation of pulmonary embolism. Two have remained free of symptoms for two and seven years (O. O. and P. H.). The other patient (A. W.) was well for twelve years and then returned with a brief episode of bleeding from the upper gastrointestinal tract. An esophageal ulcer was suspected from the esophagogram but the esophagoscopist found no evidence of esophagitis or esophageal ulcer. However, he did notice regurgitation of gastric contents into the esophagus.

In general, the results of treatment of those patients with significant esophageal shortening are disappointing. The only two operative deaths in the entire series of 109 patients with hiatus hernia occurred in this group. The only satisfactory results followed hiatal enlargement without replacement of the stomach to the abdomen, but this is not of statistical significance.

A tabulation of the late results of treatment of the various symptom categories of patients is presented in Table III. The patients listed as *relieved* were completely free of the dominant symptoms which led to hernial repair. Those patients considered *improved* were largely free of symptoms, but presented some complaints. Late postoperative incisional pain was fairly frequent in patients who had thoracic incisions. This complaint was not tabulated in the evaluation of late results.

In the thirty-nine patients listed in the *dyspepsia* category, late evaluation revealed that twenty-four considered themselves to be relieved of their symptoms, four stated that they

TABLE III
LATE RESULTS OF TREATMENT (78 PATIENTS)

Indications for Treatment	Total	Relieved	Improved	Unchanged
Dyspepsia	39	24	4	11
Acute hemorrhage	4	3	0	1*
Chronic anemia	14	11	2	1†
Esophageal dysfunction	16	6	7	3
Pain of anginal type	5	1	4	0
Total	78	45	17	16

* Recurrent hematemesis from esophageal ulcer occurred twelve years postoperatively (A. W.).
† One patient's hemoglobin was 9.3 gm. per cent due to bleeding diverticulitis (L. G.).

were significantly improved following hernioplasty and eleven believed that the operation had not benefited them. Most of the fifteen patients listed as unchanged or improved were initially relieved following hernioplasty but developed recurrent or new symptoms months or years later.

The results obtained in fourteen patients who were operated upon because of chronic blood loss anemia are presented in tabular form in Table IV. In four additional patients operation was indicated because of acute blood loss. Fourteen patients who had no further bleeding clinically and late hemoglobin levels which exceeded 12 gm. per cent were considered relieved. A patient (L. G.) listed as unchanged in Table III was relieved of blood loss due to hiatus hernia but seven years following operation was found to have a hemoglobin of 9.3 gm. per cent and blood loss consisting of bright red rectal bleeding apparently related to diverticulitis. Two patients listed as improved had no clinical evidence of blood loss but their hemoglobin levels were 11 to 12 gm. per cent. The importance of long-term evaluation of results of operation is evident in another patient (A. W.), who was considered unrelieved in Table III, because of recurrent brief hematemesis from esophageal ulcer twelve years after operation. Operative intervention was not necessary in this patient at the time of this episode of bleeding. Vagotomy was performed in three patients listed in the *bleeding* group including one patient with relief of anemia and recurrence of the hiatal hernia. The clinical results of treatment are good in this category of patients.

Relief of symptoms was complete in six and incomplete in seven of the sixteen patients whose primary complaints were categorized as due to dysfunction of the esophagus. Three patients stated that the operation did not help them because dysphagia, regurgitation, or other symptoms recurred. The association of other abdominal disease (cholelithiasis and duodenal ulcer) was particularly frequent in this group of patients and may have some bearing upon the late results which are nearly as unsatisfactory as the results of treatment of the patients listed in the *dyspeptic* group. Only six of the sixteen patients had lasting and complete relief of their initial symptoms of esophageal dysfunction.

The five patients who initially complained of severe chest and shoulder pain were uniformly relieved of the severe pain by repair of their hiatal hernias. However, four of the five patients complained of some discomfort and therefore are considered to be improved rather than completely relieved.

If we are optimistic in evaluating the results of treatment in all categories of patients and consider the patient with late anemia from diverticulitis as well as the patients listed as improved to have obtained good results, we are still confronted with a disconcerting 19 per cent in which there was failure to obtain symptomatic relief. If we are more pessimistic and consider good results to have been obtained only in the *relieved* group, there is a 42 per cent incidence of treatment failure.

TABLE IV
CHRONIC ANEMIA ASSOCIATED WITH HIATUS HERNIA*

Patient	Cause of Bleeding	Hemoglobin Value (gm. %)†		Follow-up Interval (yrs.)
		Preoperatively	Postoperatively	
J. D.	Unknown	4.8	12.5	11
M. A.	Unknown	6.5	12.4	7
F. D.	Esophageal ulcer	9.3	13.0	2
A. K.	Unknown	4.5	13.5	7
E. E.	Gastritis, esophageal ulcer	8.9	14.5	4
C. F.	Gastritis	8.5	12.0	5
M. L.	Unknown	8.0	11.0	2
L. G.	Unknown	7.5	9.3‡	7
A. C.	Esophagitis	10.5	12.4	8
N. G.	Unknown	7.5	13.0	7
N. S.	Unknown	10.5	11.9	4
I. H.	Unknown	9.5	13.0	4
A. D.	Unknown	8.6	15.0	4
C. S.	Unknown	8.5	12.6	3

* The four patients with acute bleeding are not included as their preoperative hemoglobin levels were not indicative of the extent of blood loss.
† Preoperative average, 8.1 gm. per cent; postoperative average, 12.8 gm. per cent; average length of follow up, 5.4 years.
‡ Excluded from the averaging as the anemia was due to bleeding diverticulitis.

It is noteworthy that, except for the *bleeding* category in which hemoglobin measurements were made, the evaluation was of subjective complaints. The results of treatment were best in the patients with acute hemorrhage and chronic anemia whose hemoglobins were evaluated objectively. Perhaps indifferent treatment results should have been expected upon late evaluation of this generally doleful group of aging patients with frequent associated gastrointestinal and biliary tract disease with a high incidence of obesity, poor tissue strength and other degenerative disorders. Further, evaluation is made difficult by the apparent high incidence of functional overlay concerned especially in the dyspeptic patients.

Recurrence of hiatal hernia in the seventy-eight patients studied gives us more cause for concern. Late barium studies were made in twenty-nine patients revealing recurrence diagnosed roentgenographically in fourteen or 48 per cent. The incidence of recurrence bore no significant relationship to the surgical approach (thoracic or abdominal) or to the technic of hernioplasty. Curiously, the presence of recurrent hernia had no significant relationship to recurrence of symptoms. We cannot explain this apparent inconsistency.

We are inevitably led to the conclusion that some factor concerned in recurrence of herniation and of symptoms is not being recognized consistently. Progressive tissue deterioration or increased intra-abdominal tension are factors which might be concerned but influences about which little can be done. Because delayed gastric emptying and gastroesophageal reflux could be concerned in both recurrence of herniation and of symptoms, a routine treatment by means of trans-abdominal hernioplasty utilizing the Allison principle of crural approximation [3,7] and vagotomy-pyloroplasty [2,4] was begun in one of the services (Veterans Hospital) in March 1959. So far eight patients with sliding hiatal hernias have undergone this procedure. One died postoperatively of coronary occlusion. The early postoperative results in the remaining seven patients are encouraging but no conclusions may be drawn as to the true worth of this treatment for several years.

SUMMARY

One hundred patients with apparently symptomatic hiatus hernias were operated upon during the ten year period from 1947 to 1957. The patients were categorized according to the primary indication for operation into the following groups: dyspepsia, bleeding (acute hemorrhage and chronic anemia), esophageal dysfunction, and pain of anginal type.

The source of bleeding was ascribed to esophagitis (with or without distinct esophageal ulcer) or gastritis (edema, congestion and hemorrhage of mucosa of herniated stomach revealed on biopsy) except for one case of gastric ulcer in the herniated stomach.

Late follow-up studies in seventy-eight of ninety-eight surviving patients revealed a distressingly high incidence of recurrent herniation and/or symptoms despite earlier satisfactory results. The best late results as measured by clinical evaluation were in those patients who were operated upon because of pain of anginal type, acute bleeding or chronic anemia. Less favorable results were attained in patients who initially complained of symptoms of esophageal dysfunction and the least favorable results in patients whose preoperative symptoms were sufficiently nondescript to be considered dyspeptic in type. In some patients in this latter group it is suspected that the symptoms were partly or entirely due to some disorder other than hiatus hernia.

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Common Misconceptions in Radiation Therapy*

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EDITORIAL COMMENT

This report of Dr. Buschke is very apropos to the times. It shows that radiation therapy has become an important specialty just as many areas in surgery have during the past few years. It has been my pleasure to work rather closely with Dr. Buschke for the last five years. If he can get his ideas across to both surgeons and radiotherapists, perhaps we will see fewer cases of cancer of the breast treated by inadequate simple mastectomy and inadequate postoperative radiation therapy in the future. We are seeing entirely too many of these cases today. Certainly, we as surgeons should not try to tell a well trained radiologist how much radiation therapy to give to a certain lesion any more than he would try to tell us how much or what type of surgery to perform. However, I wish to give an example of something which is disturbing to me. A patient with lymphosarcoma of the stomach was recently given an obviously inadequate dose of radiation therapy. The radiologist stopped the therapy because of the patient's slight nausea without making any effort to help the patient to control it. This occurred in one of the smaller communities in our area. As a matter of fact, the patient quoted the radiologist as saying that the x-ray therapy would make him very sick and there was nothing to do about it. It is quite obvious that we need more well trained radiotherapists just as we need well trained surgeons.

I have had an opportunity to operate upon patients after they have been given a course of radiation therapy by Dr. Buschke and his staff, and I have had no difficulty whatsoever with healing of the wounds.

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IN contrast to other medical specialties, clinical radiation therapy has matured from infancy into adult status within the lifetime of one generation. Many remember the time when severe mucosal and skin reactions were considered unavoidable and even desirable. We remember the disastrous late injuries, some of which we caused. The delayed clinical manifestation of radiation injuries, at times years or decades later, enhances their interpretation as unavoidable and masks their true significance as remainders from the early times of trial and error. The retarded appreciation of the need for recognition of radiation therapy as an independent specialty and for a more thorough training of radiation therapists tends to perpetuate the early inadequacies of judgment and technic. Thus, in many communities (even in recognized metropolitan hospitals and teaching institutions) physicians have never had an opportunity to observe competent radiation therapy.

A quotation from a letter of referral from one of the great teaching centers (dated December 1, 1953, twenty-five years after the roentgen unit was defined and thirty-one years after Coutard had demonstrated his first controlled inoperable carcinoma of the larynx) follows: "From September 17, 1951 to September 29, 1951 the patient received external roentgen therapy . . . utilizing the following factors: 250 kv.; 30 ma.; 50 cm. distance, ½ mm. cu. for four minutes daily for an over-all period of thirty-six minutes."

No wonder that erroneous conceptions regarding the possibilities, limitations, and risks of radiation therapy remain prevalent in the minds of many physicians. It is not sufficiently appreciated that well recognized indications and contraindications have become established in radiation therapy which have the same validity as in surgery and other older specialties.

* Read at the meeting of the Rocky Mountain Radiological Society, August 1959. The statistics of the Tumor Institute of the Swedish Hospital, Seattle, Washington which are included in this paper are based on my personal experiences while associated with that institution prior to December 1956.

The optimist feels that radiation therapy "may be tried" in almost any situation, particularly when other methods have failed. It is sometimes considered as a convenient placebo. Some seem to believe that contraindication of surgery is almost synonymous with indication for radiation therapy. Such uncritical enthusiasm was recently epitomized by a request for prophylactic irradiation for the prevention of keloid following surgery for a cleft palate in a two and a half months old infant. This request came from a surgeon who objects to irradiation of cancer of the lip in adults because of the risk of late radiation carcinoma. The present concern with genetic effects has at least silenced requests for tickling the ovaries in the treatment of sterility. These requests were followed at times by those for irradiation for castration and then for treatment to the pituitary to reduce menopausal symptoms.

The pessimist, on the other hand, is unduly apprehensive of early and late morbidity associated with irradiation, and he underrates its rather consistent efficacy in properly selected cases.

A brief analysis of at least some of the most commonly encountered misconceptions may, therefore, help us to arrive at a more realistic understanding of the present situation.

We can dispense with the problem of radiation sickness rather easily. Twenty-five years ago Coutard taught us that the incidence of radiation sickness is related to the incompetence of the radiation therapist. Radiation sickness, like the toxic effect of other potent drugs, can be prevented or minimized in most instances by adjustment of treatment technic to the tolerance of the individual patient. In 1940 Cantril [*10*] stated: "That this can be done in all but exceptional cases is not believed by the majority of therapists. Particularly skeptical are those who have never made the attempt." Patients frequently contract radiation sickness from the referring physician who has described it vividly, and they become sick before treatment is begun. The reduced volume dose for the same tumor effect with supervolt therapy has further simplified the situation and has practically eliminated radiation sickness. If it does occur, it can always be attributed to errors of technic. The confusion is well illustrated by a radiologist's letter referring a patient for supervolt therapy because medium-volt was not tolerated: "First of all, Mrs. . . . has the complexion and hypersensitiveness of a redhead. As you suspect, she tolerates radiation very poorly, and we have not been able to control her headaches, nausea, or vomiting with tranquilizers or other medication." Review of this patient's record showed that the intolerance was not related to the voltage or to the color of her hair, but to excessively large fields treated with daily doses which were too large. If we set out to do it, we can cause radiation sickness with supervoltage, too.

Even if this patient had a somewhat more than average sensitivity of the skin as some redheads and light blondes have, this has no relation to her constitutional tolerance. Incidentally, the skin tolerance of such patients, contrary to widespread belief, does not cause any particular problems if treatment is correctly adjusted to this anticipated sensitivity.

Cantril has pointed out that this problem of radiation sickness has become more serious since the advent of the tranquilizers [*13*]: "I find it increasingly more difficult to teach the concept of radiation sickness . . . The increasing importance given to pharmacologic research to provide drugs which combat nausea, etc., really does more harm than good since they cover up what may be an alarm reaction to unwarranted irradiation which could otherwise be adjusted to meet the situation." Symptoms of radiation sickness indicate that we are approaching the limits of the patient's constitutional tolerance to radiation therapy. Such warning signals should be heeded in order to avoid deterioration of the patient's general condition which may reduce his resistance to tumor growth.

The most common objections to radiation therapy are based on supposedly unavoidable late complications associated with severe damage to the vasculoconnective tissue. Vascular changes leading to fistulas; massive fibrosis initiating contracted bladder; obstruction of the rectosigmoid, ureter, and esophagus; and pulmonary fibrosis are still anticipated by some as almost unavoidable side effects. The difficulty of later surgery in heavily irradiated tissue is stressed again and again. Irradiation over cartilage, bone, vulva, and around the eyes is considered impossible without grave risks. Late cancer referable to previous irradiation is cited as contraindication to treatment. What does the record show?

In 583 patients treated for cancer of the cer-

vix at the Swedish Hospital between 1939 and 1956, there were seven (1 per cent) clinically significant instances of bowel injury due to radiation damage of the vasculoconnective tissue. One of these patients was living ten years later with a permanent colostomy; one had a resection of the small bowel which remained controlled for ten years; three with temporary colostomy remain well after five, eight, and ten years, respectively; one with a temporary rectovaginal fistula which is now closed is well after three years; and one is dead of diverticulitis. Three late bladder ulcerations (0.5 per cent) occurred in this series and healed within one year. These patients remain well. There was no vesicovaginal fistula in a patient with controlled primary carcinoma of the cervix and only one in carcinoma of the cervical stump. Fracture of the femoral neck did not occur in this series.

The Radiumhemmet has reported rectal ulceration in 2.7 per cent and rectovaginal fistula in 0.5 per cent of 3,392 cases of treated pelvic carcinoma [*16*]. This is hardly consistent with Meig's experience that "bowel injury following radiation treatment is not infrequent," [*19*] nor with his conclusions that the high incidence of "serious bowel injury in our clinic" following irradiation must be considered in an evaluation of surgical versus radiation therapy.

In my experience, ureteral obstruction due to radiation fibrosis has not occurred following the correct treatment of any form of pelvic cancer during the last twenty years. In every instance in which this possibility was considered, the following course indicated that the obstruction was caused by uncontrolled neoplastic disease in the parametrium rather than fibrosis. It is possible, however, to cause such obstruction by other technics thought to be ill advised, such as interstitial irradiation of the parametria.

I have not seen fibrosis of the bladder following external irradiation for carcinoma of the bladder (or other pelvic organs) with doses of 5,000 to 6,000 r delivered in six to eight weeks. Eight-five patients were treated more than five years ago and sixty-six more than ten years ago, with sixteen and thirteen per cent clinical cure rates, respectively. Those who remained controlled were treated with doses not in excess of 5,000 r, and they retained normal capacity and function [*5*]. That severe fibrosis can be caused is shown by one example of a patient treated in 1935, during the early days of supervolt therapy, who received what in retrospect was calculated to be about 10,000 r pelvic dose in sixty-three days. Sixteen years after treatment, the patient needed a colostomy for obstruction by rectal fibrosis and one year later he developed a ureterorectal fistula [*8*].

Severe fibrosis of the bladder has been observed more frequently following intracavitary irradiation using either a central source or radioactive solution. Intolerable reduction of the bladder capacity, bleeding, hydroureterosis, and hydronephrosis have necessitated cystectomy even in patients with controlled carcinoma. Thorough evaluation of the now known evidence has led Mackay [*18*] at the Royal Marsden Hospital to the conclusion that intracavitary therapy with single high doses of 3,000 to 4,000 r on the bladder surface (if given in four to six hours, or even 6,000 r in fifteen days, divided into three fractions of 2,000 r in two to three hours each) have caused severe mucosal damage and in some cases intractable hematuria or late fibrosis necessitating cystectomy. Prolonged irradiation, however, with surface doses of 4,500 to 5,000 r, continuously distributed over four days, has been tolerated. Bratherton [*3*] of the Manchester Institute considers 6,500 to 7,500 r surface doses, divided into two treatments of twenty-four hours' duration each within one week, as "a dosage of radiation which is near that of tolerance of the bladder." It is now recognized that heroic attempts to force the issue by exceeding the bladder tolerance lead to a point of diminishing returns and discredits radiation therapy of carcinoma of the bladder which, if properly conducted, plays an ever increasing role with well recognized indications.

That radical surgery is well possible following radical radiation therapy, without complications beyond those associated with such radical surgical procedures alone, has been discussed elsewhere in relation to combined treatment of extensive lesions of the oral cavity [*9*]. Esophagectomy with primary anastomosis following radical irradiation for carcinoma of the esophagus has been performed on two of my patients without surgical complications. A group from Memorial Hospital for Cancer and Allied Diseases recently reported a systematic approach with combined heavy preoperative irradiation followed by surgery in carcinoma of the esophagus [*4*]. In twenty patients treated in this fashion since 1956, the resectability rate was 54 per cent, and apparently no excessive surgi-

cal complications were encountered. In my experience laryngectomies following failure of radiation therapy have led to what possibly is a slightly increased incidence of pharyngeal fistulas. In the material of the Swedish Hospital between 1938 and 1957 [*11,12*], fourteen laryngectomies for uncontrolled disease were performed three to fifty-six months after irradiation. Four developed pharyngocutaneous fistulas postoperatively, but all were closed and the patients remained well.

Baclesse [*1*] concludes from his experience with forty-nine patients who had laryngectomy following unsuccessful irradiation for laryngeal carcinoma: " . . . if the radiotherapist's technique has been correct, small fields with fractionated dose, it is possible in case of failure to do a total laryngectomy under almost as good conditions as if the operation were to have been done primarily."

The common denominator of all these dreaded injuries is the radiation damage to the vasculoconnective tissue. I believe that the greatest progress in radiation therapy during the last twenty years lies in our increased ability, which was acquired empirically, to protect the vasculoconnective tissue by two technical modalities: greater fractionation of treatment in time and supervolt therapy. Greater fractionation is probably the more important. We have learned that the tumor effect on most epidermoid carcinomas is not compromised by prolongation of total treatment time up to eight or even twelve weeks, but that the damage to the vasculoconnective tissue is very greatly reduced. This was shown recently by Baclesse's analysis [*2*] of some 2,000 cases and is in agreement with my previous and more recent experiences with treatment using supervoltage [*9*]. Sufficient protraction significantly and often critically increases the differential between tumor vulnerability and that of the normal structures, which is the aim of successful radiation therapy. To cite disasters such as those mentioned above as serious contraindications to modern radiation therapy is equivalent to telling a surgeon that amputation is contraindicated because of the almost certain death from septicemia.

That lesions closely overlying cartilage or lesions originating in the more sensitive mucous membranes, such as vulva, female urethra, or anus, cannot be treated by radiation therapy because of the low tolerance of these tissues is still a commonly encountered error. In addition to the necessary protraction of therapy, it is even more important in these situations *to select the optimal quality of radiation*. Frequently such lesions are treated with low voltage irradiation because of their rather superficial location which does not necessitate radiation of greater penetration. This accounts for the poor tolerance. Radiations of shorter wave lengths, such as medium voltage radiation in the treatment of carcinoma of the auricle or vulva, are not selected because of their better depth dose, which is unnecessary and might even be disadvantageous, but because of the better tolerance of tissue for this quality. While radiation therapy is not the procedure of preference for vulvar carcinoma if surgery is feasible, it can be used at times to great advantage when surgical removal either is not possible or would lead to considerable mutilation by removal of the urethra [*7*].

It is well recognized by experienced therapists and surgeons that lesions in the region of the eye can be treated by radiation therapy with complete protection of the eye. Excellent cosmetic results are obtained with even large carcinomas involving the eyelids where radiation therapy in many instances has undoubted preference over plastic surgery.

The problem of the development of cancer in irradiated tissues is closely related to the problem of severe damage to tissue. Most cancers that can be interpreted as late radiation effects have occurred in severely changed tissues with the tissue damage present for a long period of time. Its occurrence following technically correct radical therapeutic procedures is extremely rare, and the interpretation in many recorded instances is debatable. In the material from the Swedish Hospital, there was one case in 134 cancers of the lip treated between 1938 and 1950 which can be interpreted as either radiation induced or new carcinoma arising in the gingiva five years after what we now consider as excessive irradiation [*8,20*]. One patient treated for carcinoma of the cervix developed a superficial carcinoma of the vaginal portion of the cervix and vaginal mucosa sixteen years after the original treatment. One patient with advanced papillary transitional cell carcinoma of the bladder, treated twenty-two years ago, is now dying of what can be interpreted as radiation induced epidermoid carcinoma of the lower bladder segment, again within an area of marked radiation change.

I do not have to go into details as to the question of sarcoma of the bone induced by radiation. The reported cases in the literature are well known. It is rather surprising to note their rarity, considering the many patients treated for carcinoma of the breast or cervix who have received large doses to bone and have been under close observation for periods of from two to three decades. I have seen only one patient with what can be interpreted as radiation induced sarcoma of the bone in a clavicle ten years after treatment of carcinoma of the upper thoracic esophagus.

From a critical analysis of the material available both in the literature and in our own experience, it is safe to state that the incidence of cancer induced by radiation following a single course of technically correct therapy is so small that it should not enter into clinical considerations. After all, medicine is (to quote Osler): "an art which consists largely in balancing probabilities." For a proper interpretation of such occurrences, it is also of interest to note that in 212 patients with carcinoma of the cervix treated at the Swedish Hospital between 1935 and 1949 who had survived five years, 7 per cent developed a second major, histologically different type of cancer somewhere else in the body obviously not related to the original cancer or the irradiation. In contrast only 4 per cent of the patients with cancer of the cervix controlled after five years died of reactivated disease at a later time.

This leads me to the next problem: the common misconception with regard to so-called "radiosensitivity" which is closely related to the question of the "cancerocidal dose."

Some pathologists seem to be endowed with an uncanny clairvoyance: by looking at a section under the microscope they can foretell whether the remaining portion of the tumor in the body is likely to be destroyed by ionizing irradiation with sufficient certainty to include in their report a statement of the "radioresistance" or "radiosensitivity." Unfortunately, these are quite often the same pathologists who may have difficulty in distinguishing an amelanotic melanoma from an undifferentiated epidermoid carcinoma. Experienced tumor pathologists admit that there is nothing in the microscopic structure which in itself indicates the degree of radiovulnerability. From hearsay, they have learned that certain histologic varieties of tumors respond and others do not.

"Radioresistance" of adenocarcinomas as contrasted to "radiosensitive" epidermoid carcinomas is still frequently assumed. This historical adage can be traced to Regaud who "from the very beginning of radiotherapy, in the course of the year 1919 in particular, declared . . . that radiation would be efficacious only in certain histologic forms. Without this scientific conception, without this foresight of facts, all progress would have been most difficult, and the discouragement in the presence of repeated failures in some histologic forms would have paralyzed for a long time the development of radiation" [*14*]. Time has indeed proved that radiotherapy measured by curability has accomplished its most consistent success in the treatment of epidermoid carcinomas. However, it is not true that glandular carcinomas are less responsive, and we have learned by now that the reasons for preferring surgery in operable adenocarcinomas, such as breast, rectum, or endometrium, are other than their radiovulnerability which is often as great as and sometimes greater than that of some of the epidermoid carcinomas. The reasons for the preference for surgery in these lesions are rather those of anatomic location or extension. All of these carcinomas require, on the average, doses for sterilization which can safely be introduced only in a relatively limited volume of tissue. A small carcinoma of the stomach, when recognized, or a carcinoma of the rectum involves a considerably larger volume than even an advanced carcinoma of the larynx or pharynx and usually has spread to lymph nodes by the time of diagnosis. A carcinoma of the endometrium is as responsive as a cervical carcinoma, but we prefer surgery because of the greater difficulty of determining the accurate size and form of the uterine cavity, which makes proper intracavitary treatment more difficult and less reliable. It is important to recognize these reasons for surgical preference because radiation therapy may still have a very useful place in inoperable situations for palliation or retardation of the disease in many glandular carcinomas.

Another favorite fallacy is the assumption of a parallel between the degree of histologic differentiation and radioresistance, particularly of epidermoid carcinomas. The gross characteristics of a lesion which cannot be correctly interpreted from the histologic analysis of a small biopsy often permit us a more accurate appraisal of the anticipated response than the

histologic structure. An exuberant exophytic papillary growth in the epiglottis is quite a different disease from a flat, deeply infiltrating ulceration. Yet the microscopic findings in a small biopsy may not differ markedly. The particularities of the tumor bed and the precise point of origin of a neoplasm may be of far greater importance for its radiovulnerability than the histologic type or differentiation. A carcinoma of the aryepiglottic fold has a fairly good prognosis, while treatment of a carcinoma of the neighboring pyriform fossa almost universally fails. The same is true for the difference between carcinoma of the tonsil and the tonsillar pillar. Coutard stated as early as 1937 that, "In the buccal cavity, the larynx and pharynx, there exist neoplasms of frequent curability when the origin is situated at a definite point. But when the point of origin is several millimeters distant, even though the histologic form is almost similar, failure is the rule" [*14*].

The terms "radiosensitivity" and "radioresistance" are relative if they mean anything from a prognostic point of view. As mentioned before, improvements in technic have brought a number of epidermoid carcinomas which previously were unfavorable objects for radiation therapy within the realm of curative therapy by increasing the differential between vulnerability of the tumor and the tumor bed. We are also slowly learning that some mesenchymal malignant neoplasms, such as fibrosarcoma, neurogenic sarcoma, or chondrosarcoma, are not so "radioresistant" under certain circumstances as the textbooks indicate and may show clinically significant responses to sufficiently high doses such as those that can be given with greater safety using supervolt technics [*6,15*].

Finally, it is impossible to predict the response and the prognosis in the individual case prior to the observation of actual changes as observed during treatment even for those tumors which we generally consider readily amenable to radiation therapy.

These observations also imply that there is no known cancerocidal dose for any particular tumor. Again, we know in general terms the approximate level of dose needed to destroy tumors of certain histologic varieties. The dose necessary for a tumor in an individual patient can only be appraised by the observation of response, and we find surprises in either direction. Baclesse recently made the following statement regarding epidermoid cancer of the larynx: "Theoretically the choice (of surgery vs. radiation therapy) should be guided by the radiosensitivity of the tumor. In fact, nothing permits one, *a priori*, to estimate this radiosensitivity with certainty. The histologic formula on which we originally placed such reliance has only limited value. There is only one method available: the proof of the radiotherapeutic trial" [*1*].

Lederman concurs: "Of far more importance to the radiotherapist than the possession of special radioactive isotopes or modern supervoltage equipment is his ability to use a laryngeal mirror and to individualize treatment . . . A standard tumour does not exist nor is there any special tumour dose, the administration of which is likely to be regularly successful. In these circumstances, the best chance of success does not lie in forcing the patient to do battle with a prescribed 'lethal tumour dose' of radiation, but in individualizing treatment according to the patient's needs. To this end, regular and frequent examination of the patient by the radiotherapist is essential. The radiotherapist who cannot and will not examine the larynx regularly fails in his duty and may well reduce his patient's chance of success as well as add to the risk of treatment" [*17*].

The mystic figure of 6,000 r has somehow appeared recently as a cancerocidal dose for most epidermoid carcinomas as well as for some other neoplasms. I believe that the reason is rather the realization that this dose, with a fractionation of about 1,000 r per week, is approximately the level tolerated by the vasculoconnective tissue. Thus, it may represent an approximate ceiling for safety but does not indicate the dose necessary for tumor control.

I have mentioned only some of the more commonly observed misconceptions. One fundamental error from which many of the others probably derive is the idea that radiation therapy is merely a physical science, that its purpose is to introduce as accurately as possible a prescribed amount of physical energy into a certain volume of the human phantom for the treatment of a tumor catalogued as "radiosensitive." This is comparable to treatment of cardiac disease with a routine dose of 300 mg. of digitalis daily to a total dose of 6 gm. in twenty days. This erroneous interpretation has two consequences: it leads to an exaggerated emphasis on the importance of the machine available without appreciation of the fact that

the prognosis is determined in decreasing order of importance by the biology of the disease, the competence and skill of the therapist, and least significantly, by the apparatus; it explains the remarkable situation in which the pathologist, surgeon, neurosurgeon, gynecologist, orthopedist, dermatologist and laryngologist seem to have a more thorough knowledge of the indications and technics than does the radiotherapist and often believe themselves to be competent to supply him with quite detailed prescriptions which have been gathered from the literature. The less such an adviser is biased by experience the more precise his predictions. Only the osteopaths have always regretfully respected my admitted ignorance without trying to educate me.

Exact physical control is essential (even more so with the use of radiation in the super- and megavolt range—cobalt, betatron, linear accelerator) but must be subordinated to skilled clinical judgment comparable to the place of anesthesiology in surgery or pharmacology in medicine. Clinical radiation therapy is essentially not a physical science but a clinical art. The therapist is primarily a physician who must understand and appreciate the intricacies, vagaries, and unpredictabilities of a biologic system.

As a matter of historical fact, radiation therapy, like other clinical specialties, originally developed empirically and progressed by trial and error. All essential, clinically important experiences were available thirty years ago before the roentgen unit was defined. The results of treatment of carcinoma of the cervix were published by Lacassagne in 1926. This was two years prior to the definition of the roentgen. His results compare favorably with the best attained today. The understanding of the physical details and the more exact explanation of the many, well known empirical observations followed in retrospect.

Undoubtedly many of the cited misconceptions among radiologists and other physicians are based on observation of and experience with inadequately executed radiation therapy. When radiation therapy is evaluated in regard to its curative results and to the associated morbidity and tissue damage, the possibilities, limitations, and risks are not always measured by evaluation of procedures as executed by well trained and experienced specialists as surgical results usually are. With continued improvement of radiation therapy itself, particularly through the training of a greater number of competent therapists and the organization of more departments of radiation therapy in the larger hospitals, the trend toward better understanding of the place of radiation therapy in the treatment of cancer will undoubtedly continue. The experience has been universal that mutual understanding and appreciation are proportionate to the competence of the cooperating surgical and radiotherapeutic specialists.

If we sometimes believe that progress is too slow, we should remember how young the specialty of radiation therapy really is as compared with surgery. We should not forget Noah Webster's wisdom expressed in 1783 in the first edition of the *Speller*, which was recently brought to our attention by Cushman Haagenson: "To attack deep rooted prejudices and oppose the current of opinion is a task of great difficulty and hazard . . . Even errour becomes too sacred to be violated by the assaults of innovation."

Acknowledgement: I am grateful to the late Dr. Simeon T. Cantril, Director of the Tumor Institute until his death in September 1959, for supplying me for the preparation of this paper with those data which had not been published previously. Dr. Cantril reviewed the completed manuscript in July 1959, suggested its publication, and authorized inclusion of these data in a letter dated August 11, 1959. I also wish to express gratitude to the present Director of the Tumor Institute, Dr. Orliss Wildermuth, for his permission to use this material.

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Cancer of the Colon

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PATIENTS with cancer of the colon may be divided into two groups: The first group includes all cases in which the tumor of the colon causes acute intestinal obstruction. The second group includes the remaining patients. In these, the tumor is detected only by clinical examination. Obviously the clinical picture is quite different in each group.

The first group comprises the greater number of patients in our experience at the Sklifosovsky Institute in Moscow. Indeed, of 500 patients admitted to the Sklifosovsky Institute from 1935 to 1959, 347 (69 per cent) were hospitalized for urgent operative treatment. Only 153 (31 per cent) were hospitalized for routine evaluation and treatment for suspected carcinoma of the colon. Of the 314 patients who underwent radical operations, eighty-six had had a prior emergency operation for intestinal obstruction. (Table 1.)

Although the composition of this group of patients was peculiar to the Sklifosovsky Institute where predominantly emergency cases are treated, it reflects the actual percentages among all such patients. Smiddy and Goligher of England (1957) mention in their statistical data that 18 per cent of 1,000 patients had ileus. Brunsgaard of Norway (1956) refers to the fact that one-third of their patients were hospitalized with acute intestinal obstruction. Burgess and Barling of Manchester (1923) mention the figure 35 per cent in this connection.

TABLE 1
CANCER OF THE COLON
(Sklifosovsky Institute)

No. of Patients	
Male	211
Female	289
Total	500
Admission Status	
Emergency	347
Routine	153
Type of Operation	
Radical	314
Mortality	7.4 per cent (23)
Palliative	186
Mortality	32 per cent (58)
Anastomosis	66
Mortality	15
Ileostomy or colostomy	81
Mortality	32
Laparotomy	39
Mortality	11

These facts express the peculiar nature of cancer of the colon. Its symptoms develop slowly and a timely diagnosis is made only with extreme difficulty. Its course, therefore, resembles that of cancer of the esophagus in this respect. Indeed, we observed that in three of every four patients the tumor of the colon was detected only when the lumen of the bowel was completely obstructed so that even the passage of gas was impossible.

Most of our patients were between fifty and eighty years of age. However, there were thirteen patients less than thirty years old. We operated on one boy twenty and a girl eighteen years of age. As was to be expected, the obstructing tumor was located in the left half (predominantly in the sigmoid) of the colon in 80 per cent of all cases. Only in eleven patients was the obstructing tumor in the right hepatic flexure.

Of course these were far advanced forms of the disease. According to general opinion, at least a year must elapse from onset of disease before the tumor causes intestinal obstruction. Nevertheless, as we shall see later, an extensive resection of such a tumor is not only practicable if there are no metastases, but also the patient may hope for considerable longevity after the radical operation.

In considering the course of the disease, patients should be separated into three groups. The first, or dyspeptic group is the largest one.

Included here are patients who complain of indefinite pain in the abdomen accompanied by some muscle spasm. Chronic appendicitis and cholecystitis are often suspected in such cases. Of 122 patients subjected to radical operations for lesions of the right half of the colon, twenty-eight had been admitted to the Sklifosovsky Institute with quite different diagnoses. According to data published by Mayo and Delaney (U.S.A.), the initial diagnosis was not confirmed in 250 of 1,000 cases.

The second group is characterized by fatigue and pronounced anemia without visible blood loss and without pulmonary symptoms. The hemoglobin level may drop to 50 per cent. This anemia is apparently of toxic origin and associated with the destroide tumor. It is peculiar to lesions of the right half of the colon. Observations from our patients show that the average hemoglobin level with lesions on the right side was 54 per cent. With lesions of the left half of the colon it was 60 per cent.

The third group consists of patients with distinctly palpable tumors in the right or left iliac region. Unfortunately, these tumors are often mistaken for appendicular inflammatory masses. Sometimes actinomycosis is suspected. As a result of these misdiagnoses, valuable time is lost in temporizing. In view of this an exploratory laparotomy is advisable if there are clinical symptoms of tumor even though no lesion is seen by roentgenography.

In lesions of the left half of the colon, the predominant symptoms result from narrowing of the bowel lumen. Constipation is observed in 60 per cent of patients. Abdominal pain is invariable with the lesion in any location in the colon. Although cancerous tumors may develop anywhere in the colon, they are found most often in the distal sigmoid. Here stenosis develops quite often. Cancerous tumors of the cecum and ascending colon occur less frequently.

What methods of treatment should be used in the treatment of cancerous lesions of the colon? In the presence of acute intestinal obstruction it is not advisable to perform a primary resection. The ascending colon is greatly distended and the blood supply to its wall is markedly impaired. This situation may result in rupture of the suture line after tumor resection. Whether one performs end to end or side to side anastomoses, primary resection in the face of acute intestinal obstruction usually results in peritonitis.

In the case of the left sided tumor with obstruction, cecostomy construction is the first step. The use of transverse colostomy as recommended by some surgeons has not been justified. Cecostomy with subsequent irrigations usually decompresses the bowel after several days, even when the tumor is located at the rectosigmoid junction. The cecum is opened on the second or third day. Then vigorous preparations are made for the radical resection which is performed no less than ten days later. In the case of acute intestinal obstruction and tumors on the right side, an ileo-transverse colostomy is constructed first. Radical resection is then performed ten days later. (Fig. 1A and B.)

The following measures are of *prime importance:* (1) adequate hydration, (2) high protein diet, (3) preoperative blood transfusions, (4) thorough bowel decompression, and (5) bowel sterilization (neomycin by mouth over a two day period).

With tumors on the right side, this is the type of radical operation we use: The entire right half of the colon is resected followed by an ileo-transverse colostomy. (Fig. 1C and D.) This operation was proposed by Fridrich in 1904. In this operation the following principle is used: The larger the resected portion of colon, the less dangerous the operation. Consequently, it is necessary to remove the cecum, ascending colon, the hepatic flexure, and part of the transverse colon. We usually use a side to side anastomosis in joining the small intestine to the colon. Other surgeons prefer the end to end technic.

With tumors on the left side, it is also necessary to remove a large portion of bowel. Here we try to bring the mobile transverse colon down to the remaining sigmoid. It is necessary to resect the splenic flexure, the descending colon and the sigmoid. The mesentery must be incised and the lymph nodes removed from along the inferior mesenteric artery up to its origin. The latter area is the so-called "armpit of the peritoneal cavity." However, if the tumor is situated in a long sigmoid loop, the operation performed is an extensive resection. We believe that anastomosis is undoubtedly preferable to other types of end to end anastomosis in this situation. Thus, in the case of acute intestinal obstruction with a left sided tumor, the operation of choice is a *classical three stage radical resection* as described by

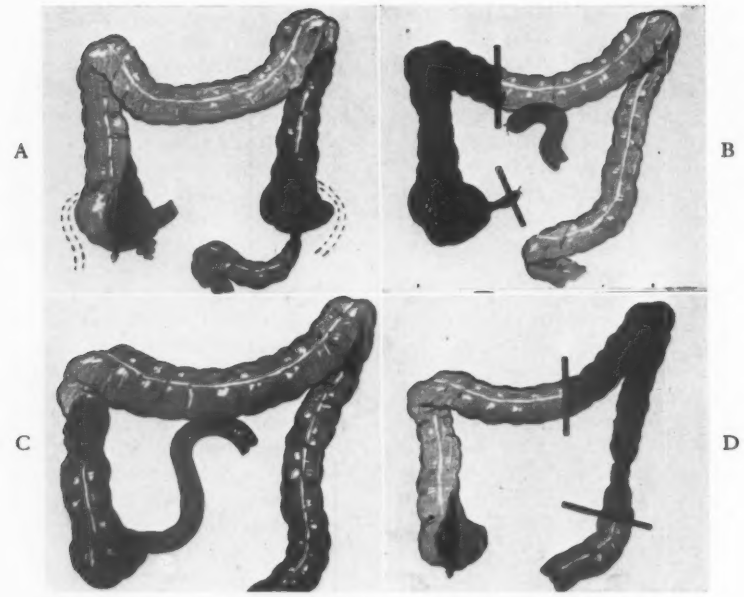

FIG. 1. Two types of initial operation for acute intestinal obstruction are shown in A and B. A, first stage cecostomy. B, first stage transverse colostomy. C and D show two types of radical operation. C, resection of the right colon with ileo-transverse colostomy (122 cases with a mortality of 7.3 per cent). D, resection of the left colon with end to end anastamosis and preventive cecostomy (192 cases with a mortality of 7.4 per cent).

Schloffer. The third stage is the closure of the cecostomy. This is done two to four weeks after colon resection. With acute obstruction and a tumor on the right side, a two stage operation is used. A preliminary ileo-transverse colostomy is followed in ten days by radical bowel resection.

When no obstruction is present, or if the obstruction is only partial, it is advisable to perform a single stage operation after thorough preparation and clinical evaluation. However, with an obese patient and a large tumor on the left side, a preventative cecostomy is advisable when even the slightest technical difficulties arise. Construction of a cecostomy requires only a few minutes. It insures decompression of the bowel, and thus a firm union at the anastomotic site.

DATA

In the course of twenty-five years (1935–1959) 314 patients with cancer of the colon had radical operations performed at the Sklifosovsky Institute. (Figure 1C and D.) Twenty-three patients (7.3 per cent) died. Included in this group of 314 were eighty-six patients who had acute intestinal obstruction prior to operation. Of these eleven had right sided lesions. One of these eleven died. The mortality rate for our two stage operation then was 11.1 per cent. The remaining seventy-five patients with acute intestinal obstruction had lesions on the left side. Here there were five deaths, making our mortality rate 6.6 per cent for the three stage operation. The over-all mortality rate for the eighty-six patients with intestinal obstruction was 7 per cent.

One stage resections were performed on 228 patients without acute obstruction. Here the mortality rate was 7.4 per cent (seventeen patients). It is noteworthy that, following the twenty-five single stage resections of the left half of the colon with preventative cecostomy, there were no postoperative deaths. Following 117 such resections, without cecostomy for cancer on the left side, nine patients died (7.7 per cent). Following 111 similar operations for cancer on the right side, eight patients died

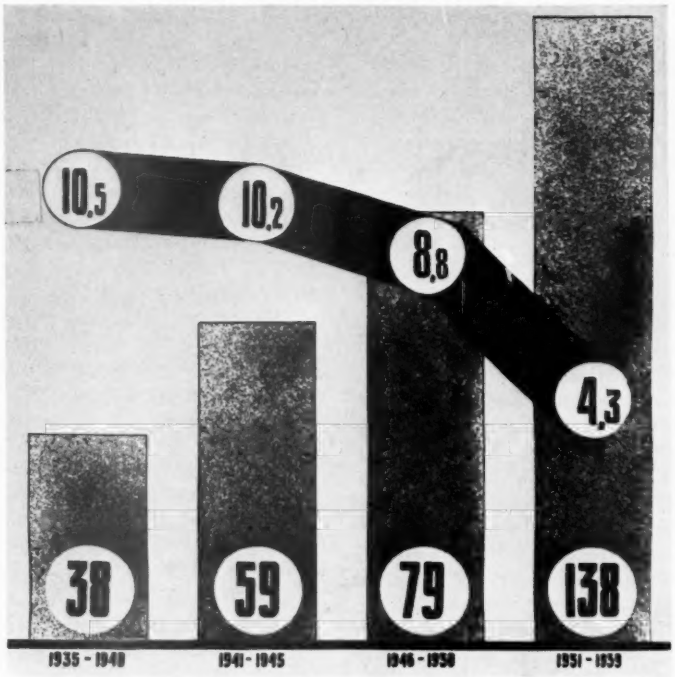

FIG. 2. Radical operations for cancer of the colon at Sklifosovsky Institute from 1935 through 1959. Curved dark line shows mortality (per cent).

(7.2 per cent). During the last nine years (1951–1959) the number of radical operations for tumors in any area of the colon has greatly increased. During the same period we have reduced the postoperative mortality to 4.3 per cent (138 patients, with six deaths as shown in Figure 2).

We are quite pleased with the long term results following our radical resections for cancer of the colon. From replies to our inquiries, we find that sixty patients survived up to three years, thirty-one patients survived from three to ten years, and thirteen patients survived from ten to sixteen years. Thus, of the group replying to our inquiries, more than 40 per cent (forty-four patients) lived from five to sixteen years following operation. This result was achieved in spite of the fact that almost half of the follow-up group had acute intestinal obstruction at the time of their first operation.

SUMMARY

1. Improvements in methods for timely diagnosis of colon cancer have fallen far behind the considerable achievements in the operative treatment of this malignancy.

2. Roentgenography of the colon and sigmoidoscopy should be used more often in the examination of patients.

3. Cancer of the colon complicated by acute intestinal obstruction, is best treated by a two or three stage resection.

4. Primary resection should be used in all other cases.

5. Our mortality rate for the 138 radical resections of the past nine years was 4.3 per cent.

6. The immediate and long term prognosis for colon cancer treated with radical resection is better than that following similar operations for cancer of the stomach and more especially of the esophagus.

Traumatic Injuries to Abdominal Organs

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THE following report deals with injuries to the gastrointestinal tract, the liver and the spleen. The cases presented were treated at The New York Hospital during the years from 1932 to 1958. Table 1 shows the incidence of blunt and penetrating trauma and the mortality for the separate categories from 1932 to 1940 and from 1940 to 1958.

The diagnosis was proven at operation or autopsy in all cases. Some of the patients were never seen by a surgeon as a surgical condition was not suspected. Eight of the cases reported occurred while the patients were hospitalized for diagnostic work up. The injuries which occurred in the hospital varied from delayed ruptures of the liver to perforations of the colon with the proctoscope.

TABLE 1
TRAUMATIC INJURIES TO THE ABDOMEN (1932–1958)

Type of Trauma	1932–1940			1940–1958		
	No. of Patients	Deaths		No. of Patients	Death	
		No.	%		No.	%
Blunt						
Solid viscera	4	2	50	10	3	33
Hollow viscera	1	1	100	6	0	0
Penetrating						
Solid viscera	3	0	0	6	1	17
Hollow viscera	7	2	29	14	3	21
Other*	3	1	33	6	0	0
Total	18	6	33	42	7	17

* This category is composed of penetrating wounds without trauma to hollow or solid viscera.

SPLENIC INJURIES

Injuries to the spleen cause death through blood loss. When penetrating injuries occur in the region of the spleen, it requires little imagination to make a presumptive diagnosis and an exploratory laparotomy frequently is indicated without the need for differential diagnosis.

When blunt trauma has been experienced, when there is no history of trauma or when the trauma is several weeks in the past, the differential diagnosis assumes a more acute role. It is debatable if a so-called true spontaneous rupture [*12*] of the normal spleen ever occurs. Minimal trauma may sometimes cause this. Two of our patients fell into this category and both were operated upon with the diagnosis of ruptured or strangulated hollow viscus.

Several factors probably are involved in how easily the organ is injured. Large spleens are more liable to rupture than small ones and a blow to the side with the elbow was a well known method of assassination in areas where malaria was endemic during the Middle Ages.

Quite often the spleen is intimately attached to the left dome of the diaphragm and sudden respiratory efforts associated with some trauma may detach part of the organ or shell it entirely out of its capsule as occurred in one of the patients discussed herein. The rupture of the leukemic spleen which occasionally occurs from the mild effort of turning in bed is perhaps in a different category but may still pose a problem for the surgeon. Subcapsular bleeding and delayed rupture form still another category. Most often the trauma resulting in rupture of the spleen is fairly violent and usually occurs to the left side of the lower chest or hypochondrium. Sometimes ribs are broken.

It is hardly possible to suspect a ruptured spleen unless a history of injury is given. When multiple injuries are present, the diagnosis becomes more difficult but it is still essential to

know the signs and symptoms of isolated splenic injury with hemorrhage.

The most frequent symptom is pain. If the patient is conscious and the shock of blood loss has not set in he will almost always complain of pain in the left upper quadrant. This pain is frequently referred to the left shoulder and aggravated by respiration even in the absence of fractures of the ribs. Nausea and vomiting may occur. Examination usually reveals a well localized tenderness in the left upper quadrant with referred and rebound tenderness. The spleen may be palpable, particularly if a subcapsular hematoma exists.

The signs and symptoms of blood loss are usually present. The pulse is small, thready and rapid; the face is ashen, grey and pinched; the blood pressure and stroke volume are low; and the extremities are cold and clammy.

Determinations of hematocrit or hemoglobin are usually of little value in the early stages when the decision to operate or not has to be made.

Five of our patients with bleeding from splenic rupture had hemoglobin values from 12.8 to 15 gm. per cent immediately prior to surgery and without evidence of dehydration, whereas estimates of blood found in the peritoneal cavity ranged from 1,000 to 2,500 cc. However, hemoglobin and hematocrit determinations are of value when slow bleeding occurs and paucity of deciding symptoms lead to observation and waiting. Leukocytosis occurs early in splenic rupture and is sometimes used as a diagnostic criterion.

Delayed rupture of the spleen is a term used for cases in which the initial symptoms and signs are so minimal that they escape attention. Apparent recovery results but emergent symptoms develop without new trauma and result in operation or death several weeks after the original injury. The so-called delayed rupture may be caused by recurrent bleeding into the splenic pulp and clots in different stages of organization may be found on pathologic examination. A clot may also form and close a rent in the splenic capsule only to be extruded or dislocated at a later date with resumption of bleeding.

The patient with delayed rupture has much the same symptoms as at the time of the primary injury. However, the spleen or a mass in the left upper quadrant often is palpable and a scout film of the abdomen is more likely to reveal a soft tissue mass and indentation and depression of the gastric air bubble.

The only patient among our cases of splenic injury to die was a patient who was hospitalized for fever of unknown origin. Before diagnosis was established he was found gasping in bed and died within a few minutes. Autopsy revealed lymphatic leukemia and a ruptured spleen with hemoperitoneum.

It can not be overemphasized that the treatment for a ruptured spleen can not await confirmation of the diagnosis which is often impossible to obtain or too late. Parsons [9] reported twenty-six cases of ruptured spleen and the three deaths occurred before operation could be performed. As soon as suspicion is aroused preparation for treatment must be initiated. The availability of an adequate supply of blood is of first and foremost importance. A history of trauma to the region of the spleen along with signs of peritoneal irritation in the left subphrenic area associated with the clinical signs of blood loss requires immediate operation. Persistence of signs of peritoneal irritation and slow decrease in hematocrit indicates subcapsular bleeding which also requires operation and splenectomy after due consideration. Unavoidably some mistakes in diagnosis will be made. Although we do not know the number of cases, there were some in which exploration revealed no lesion of the spleen and no surgical procedure was necessary. However, this risk must be accepted in dealing with a condition that may be as rapidly fatal as rupture of the spleen, and entirely avoidable by surgery.

HEPATIC AND BILIARY INJURIES

Whereas the problems in splenic injuries are blood loss and its direct consequences, the liver is a very vascular organ and also has vital functions in carbohydrate and protein metabolism. It excretes the bile which has markedly toxic effects when its normal passageway is disrupted and it comes in contact with unrelated and injured tissues.

The liver is particularly exposed to both blunt and penetrating injuries due to its weight, size and narrow attachments. Although its location in the right upper quadrant and the costal margin afford some protection, the position assumed at times of injury may make it possible for injurious forces applied to the other quadrants of the abdomen to reach and produce deleterious effects on this organ.

The dangers from injury to the liver are early hemorrhage, later derangement of function, infection and bile peritonitis.

The diagnosis of trauma to the liver caused by blunt force may often be quite difficult. In general the early signs and symptoms are those of pain and tenderness in the right upper quadrant which sometimes radiates to the shoulder.

If the bleeding and damage is entirely subcapsular, a hematoma with cyst formation or rupture into a biliary radicle may occur. In these cases hemorrhage into the intestine may be recurrent and troublesome (hemobilia) [*10*]. Delayed rupture of hematomas to the exterior also may occur and cause sudden death from bleeding. When rupture to the exterior occurs, the magnitude of peritoneal signs will depend on the amount of blood in the peritoneal cavity.

After the bleeding has stopped, oozing of bile continues from damaged and severed bile ducts. The amount of bile spilled into the abdominal cavity depends on two factors. If a large duct has been severed the part of the liver it drains may continue to produce bile that is liberated directly into the peritoneal cavity. If only small radicles are involved, the amount of distal obstruction determines the amount of regurgitation of bile. Perforations of the bile ducts do not heal easily and if any degree of distal obstruction exists, such as edema and swelling from contusion, leakage from even small perforations may be catastrophic.

Bile peritonitis usually has fairly serious and often fatal sequellae if not promptly treated. Absorption of the bile salts and production of the so-called cholemia is but one part. Of even more serious consequence is the frequent rapid loss of fluid into the abdominal cavity from the damaged vessels in the peritoneum. Depletion of intravascular plasma volume thus can reach a critical degree and is probably the common cause of death in patients with bile peritonitis.

The signs and symptoms of bile peritonitis resulting from small penetrating objects that do not cause extensive tissue damage may be minimal and fairly slow in becoming evident. Some pain is often referred to the shoulder from collections under the diaphragm. Otherwise, slow but steady rise in pulse rate with gradual abdominal distention from paralytic ileus, and shifting dullness may be the first signs. In the later stages the patient becomes obtunded. Dry wrinkled skin and sunken eyeballs show the evidence of loss of fluid from the intravascular compartment.

Although most of the injuries to the liver involve its substance and capsule, the brunt of the injury occasionally is borne by the extrahepatic ductal system and the blood vessels (portal and/or arterial). Trauma to the abdomen is sometimes involved in thrombosis of the portal vein and results in portal hypertension. Blunt or perforating trauma may damage the gallbladder and common duct. One of our patients, a thirty-four year old man, suffered an interruption of the common duct, portal vein and hepatic artery although the trauma to the liver was rather minimal. In cases like these necrosis of the liver substance occurs and death results from primary liver failure within a relatively short period of time. Our patient survived for two weeks, and the reason for the prolonged survival found at autopsy was an aberrant hepatic artery from the left gastric artery supplying the left lobe of the liver. This artery had escaped injury.

INJURIES TO HOLLOW VISCERA

The chief danger from wounds of the hollow viscera is peritonitis. The type of peritonitis varies. Perforation of the gastric wall in a young patient usually leads to a chemical type of inflammation, the same frequently is true for the duodenum where pancreatic and bile juices are added to the acid secretions of the stomach.

As the lesion is found more distally in the digestive tract the bacterial flora increases. Perforations in the large bowel are associated mainly with bacterial peritonitis which is often fulminating. The type of flora associated with perforation of the large bowel varies somewhat with the age of the patient, and mixed infections which are found mainly in the elderly are also prone to be more virulent and aggressive in character than in young people. The solid character of the contents of the lower bowel along with thinner walls often makes it difficult to perform satisfactory primary closure of wounds in this region, and exteriorization or proximal colostomy is required for an acceptable result. Wounds and perforations of the right colon, especially of the cecum where the content is still fairly liquid, may be subjected to primary closure if the blood supply has not been damaged.

Blunt injuries to the gastrointestinal tract deserve some additional comments and, as in

lesions of the other viscera, pose a problem different from penetrating trauma.

When blunt trauma to the abdominal region occurs, the result on the intestinal tract depends upon the force and the speed with which it is applied. All of the small intestine except the duodenum and most of the colon have fairly long mesenteries. In the absence of adhesions or bands these organs are pushed to the side and usually are not injured.

The duodenum is immobile and thus is exposed to crushing injuries against the spinal column. Part of the bowel and stomach also may be caught between the applied force and the immobile part of the skeleton and be damaged.

Rupture of these organs may occur without crushing. The lumina of the hollow viscera compose a cavity within but separate from the general abdominal cavity.

The status of the hollow organs at the time of injury greatly influences the extent of the damage to be expected. A stomach full of food, a bladder distended with urine and a colon containing large amounts of feces are much more liable to rupture from blunt or penetrating trauma than when these organs are in the empty state. Pressure differences within the abdomen are transmitted to the hollow organs where the contents may escape in either proximal or distal direction. Sudden and general application of external violence along with distention of segments of the bowel may result in intraluminal pressures greater than the bowel wall can withstand, and rupture will occur.

Delayed ruptures of the intestinal tract from blunt trauma occasionally occur. Peritonitis suddenly became apparent in one of our patients with a perforation of the stomach three days after the original injury. There are three explanations for its occurrence. Either the perforation occurs at the time of the accident and is sealed off only to break down later, or a contusion with devitalization of a part of the wall of the organ occurs at the time of the accident but loss of continuity is delayed for a period of time, in our case three days. A third possibility is the formation of a hematoma in the mesentery of these organs with thrombosis extending along the vessels supplying it and secondary gangrene.

Perforations of the rectosigmoid during proctoscopic examinations may happen in any one of three ways. The instrument itself may be forced through the bowel wall. This is most apt to occur when organic disease and fixation of the wall is present, as it was in one of our cases with lymphogranuloma. The second common occurrence is to exert too much traction when a polyp is being removed with a snare as is also illustrated in one of our patients. A five year old boy suffered a perforation of the rectosigmoid (2 by 1.5 cm.) in this way. Thirdly, an inverted diverticulum on the mesenteric border may be mistaken for a polyp and biopsied as such although we have not observed this. A perforation will occur even from the most superficial biopsy because of the thin wall of these diverticula.

INDICATIONS FOR OPERATION

The results of treatment in acute trauma within the abdominal cavity depend on a number of factors. Most important among these are involvement of more than one organ, lesions of other parts of the body, the availability of blood for replacement therapy and last but not least how soon the damage is repaired.

There seems to be little difference of opinion about the approach to penetrating abdominal wounds; almost everyone recognizes the necessity for exploration when penetration of the abdominal cavity has occurred. Occasionally, an author [*14*] implies that exploration is not imperative in the absence of peritoneal signs when the injury has been caused by a slow-moving or blunt object, but this is a hazardous contention which should be applied only when the facilities for strict and frequent observations are available. The decision as to whether or not one should operate in cases of blunt trauma is somewhat more difficult to make.

Dangers and symptoms arise from blood loss or peritonitis as has been enumerated. Shock occurring in a patient with abdominal injury may be from blood loss and/or peritonitis. Continued evidence of shock in the absence of bleeding elsewhere and after resuscitative measures indicates a necessity for exploration when signs point to injury somewhere in the abdomen. Trauma or contusion of the abdominal wall alone will give rise to pain and tenderness but will not cause the symptoms of shock to be maintained.

The symptoms and signs of rupture of the solid viscera have been indicated. Suspicion of splenic injury makes operation mandatory. Signs from the right upper quadrant do not

demand immediate exploration if they remain localized. This is especially true since most lacerations of the liver have stopped bleeding when exposed. Exacerbation of local signs around the liver demand exploration. This is particularly true if infection becomes apparent or bile peritonitis is suspected.

The condition of a patient with acute abdominal trauma requires continuous and constant observation for any changes as they occur. A soft and nontender abdomen may evidence board-like rigidity within half an hour. Many patients maintain circulatory compensation for a while even in the presence of massive bleeding. Then they may suddenly become faint, cold, clammy and have the rapid thready pulse indicative of shock.

The peritoneal signs caused by bleeding from the liver and spleen may remain localized for several hours only to cause generalized abdominal and rectal tenderness later.

The reliance on hematocrit or hemoglobin values as indications for operation are permissible only to a degree. Peripheral vasoconstriction and lack of dilution in the first hours after massive bleeding may completely mask any changes in these values. Clinical signs far outweigh any laboratory procedures in this respect. Constant close observation of the injured patients is necessary for early detection of the signs and symptoms which demand exploration.

It has been stated by some investigators that leukocytosis over 15,000 per cu. mm. immediately following a blunt abdominal injury is indicative of rupture of the spleen or the liver [*15*]. Certainly this is seen often, but the exceptions are too numerous to advocate any reliance on the leukocyte count to the exclusion of other procedures.

Scout films of the abdomen may be of great help. The evidence of free air in the peritoneal cavity or in the retroperitoneal area makes exploration mandatory. Fluid levels in the free peritoneal cavity likewise indicate the need for operation. Displacement of the hollow viscera by accumulation of blood from the spleen and liver also may be evident and helpful in arriving at a decision. Progressive ileus may be a sign of peritonitis but is also frequently found when bleeding and trauma is localized in the retroperitoneal area.

Diagnostic taps of the abdominal cavity are often used to great advantage according to its advocates. We have not used this method in the diagnosis of trauma. We are persuaded from its use in other conditions that its usefulness is quite limited and that most of the information elicited may be arrived at by other means. We also contend that the risk of false interpretation of such diagnostic taps is considerable.

PREPARATION FOR SURGERY

Every patient who enters the hospital with a history of abdominal trauma is a possible candidate for surgery. The examination of the injured has to encompass all the organs and systems of the body. A complete survey can not be adequately made unless the patient is fully disrobed.

Although the injured part requires the first attention, careful evaluation of the other systems by history and physical examination is of essence. Even though time is often short in such circumstances, knowledge of overt or latent disease of vital organs may make the difference between survival and death [*1*]. Massive intraperitoneal hemorrhage does not lend itself well to procrastination and is the most common cause for death prior to surgical intervention. Steps aimed at ensuring adequate supply of whole blood have to be taken concomitantly with the securing of airway and splinting of fractures if associated injuries exist. The placing of a large cannula in a vein in an extremity is just as important as the catheterization to look for injury to the urinary tract.

Decompression of the gastrointestinal tract by a nasogastric tube is essential in preparation for surgery and should be done immediately once the decision to operate has been made. Exposure of a ruptured spleen may be quite difficult in the presence of a dilated stomach. Paralytic ileus accompanies every abdominal exploration and this is compounded in trauma by peritoneal irritation from bile, blood or intestinal contents. Hemorrhage in the retroperitoneal space and contusion of bowel mesenteries all aggravate this situation and make it essential to maintain decompression until peristalsis is re-established. Antibiotics are of great importance in preparing the patients with peritonitis for surgical intervention. Antibiotics are of particular importance when interference with the blood supply of the liver or other severe trauma to the liver is suspected. Although it has not been proved in the human, it is well known from the experimental animal that rapid proliferation of anerobic organisms oc-

curs in liver tissue which is not receiving arterial blood. This has been suspected as the cause of some so-called liver deaths in the past following cholecystectomy but was probably caused by injury to the right hepatic artery. This complication of liver trauma may now be minimized or avoided if antibiotics are given to the patients [2–4].

SURGICAL TREATMENT

Liver and Biliary Tract. According to Sparkman, Burns was the first to attempt surgical treatment of a liver wound in 1870 [3]. The ends to be attained in the surgical treatment of these injuries is to ensure hemostasis, repair gross laceration of the extrahepatic collecting system, remove obviously dead and necrotic tissue and establish adequate drainage.

Clean linear lacerations of the liver may be sutured with deep mattress sutures, but this is usually impossible or ill-advised in ragged and extensive lacerations. Although massive bleeding is the common cause of sudden death prior to surgical intervention in injuries of the liver, it is often not as serious a problem at the time of surgery as might be expected. In a series of 829 wounds of the liver reported by Madding only 9 per cent were actively bleeding at the time of exploration [16]. When massive bleeding from a laceration in the liver substance is encountered, temporary hemostasis may be obtained by compressing the hepatoduodenal ligament between two fingers. Bleeding vessels may often be identified in the open wound and should be individually ligated. Massive lacerations or shattering of either lobe may require ligation of the corresponding hepatic artery and portal vein branch and excision of ischemic liver tissue.

Ligation of the main hepatic artery leads to necrosis of the liver unless it is performed fairly close to the celiac axis [4].

Foreign bodies introduced into liver wounds for hemostasis have not proved useful. Presumably absorbent material such as gelatin gauze or oxidized cellulose have been known to remain unabsorbed and cause cyst and cavity formations or to migrate to other organs. The formerly popular gauze pack which served as a hemostatic agent and a drain has been found to be a doubtful boon. Madding states that survival from wounds of the liver rose corresponding to the abandonment of the gauze pack in favor of more meticulous hemostasis with drains to the exterior.

Soft drains covered with rubber, multiple when needed, are essential to the proper handling of wounds of the liver. If drainage is not adequate, hematomas and bile collections with secondary infection and hemorrhage are the rule. Madding quotes Burford to emphasize the importance of adequate drainage [5]. Burford found that 25 per cent in a series of ninety-eight liver wounds presented complications after the initial treatment, and that all of these were the result of inadequate drainage. Lesions of the extrahepatic ductal system require proximal catheter or T tube drainage in addition to the conventional means already mentioned.

Late complications may arise from wounds of the liver because of so-called sequestrated pieces of liver tissue. These are pieces of liver substance which have become partly or totally severed from the main organ but remain in the wound as foreign bodies where they act as a nidus for persistent infection and as the source of repeated attacks of bleeding and drainage to the exterior [3,8].

There were five deaths in our series of thirteen injuries to the liver or biliary tract. Two of these patients died before surgery could be contemplated and diagnosis established. The primary cause of death in both was massive hemorrhage. One of these, an elderly lady, had a delayed rupture of an old intrahepatic hematoma. The liver enlargement had been recognized but the proper etiology missed. Postmortem examination revealed hemoperitoneum and a large intrahepatic hematoma with fibrous walls which had ruptured.

A second patient died from rupture of a similar old hematoma when bleeding recurred following surgery elsewhere. The death of this patient occurred ten days after surgery. Anticoagulants which were necessary for dialysis after the patient developed uremia from lower nephron nephrosis may have been a causal factor.

The fourth death resulted from necrosis of the liver following traumatic interruption of the hilar strictures. The fifth death occurred soon after exploration of a bullet wound which traversed both lobes of the liver and the stomach with three perforations of the stomach. The effect of multiple associated injuries on the outcome of liver trauma has been emphasized by Madding.

There were two complications in the course of the eight survivals in the group, both were caused by atelectasis and pneumonia.

A mortality rate of 38 per cent in this group of patients is disturbing indeed. However, all the deaths belong to the group of massive liver trauma in which any form of treatment has met with only limited success, or death occurs before treatment can be initiated.

Hollow Viscera. The treatment of injuries to the hollow viscera represent some of the earliest attempts at surgery on these organs. The main function of the surgeons of the Middle Ages was repair of trauma which occurred on the battlefields [*6*].

Paracelsus (after 1500) is said to have advocated exteriorization of damaged intestines rather than to attempt suture.

Palfyn (1650) advocated suture of bowel wounds but also sutured the damaged bowel up to the abdominal wound so that a fistula to the exterior would occur if breakdown of the closure resulted.

Soon after 1800 Dupuytren fashioned the clamps to facilitate closure of exteriorized segments of bowel, and this was the preferred method until Lembert advocated the serosa to serosa suture in 1826.

The necessity for exteriorization of segments of bowel because of trauma is more and more rare now due to knowledge of asepsis, tubes for intestinal decompression, and antibiotics which are effective against the intestinal flora.

Wounds of the stomach should always be closed primarily and the same is true for the duodenum and the entire small intestine. Damage to the duodenum [*11–13*] is particularly apt to be associated with lesions of the pancreas and the biliary tract. When the damage is extensive, a gastroenterostomy may be needed as an adjunct measure. Exploration of the duodenum should always be thorough and include examination of the retroperitoneal aspect as perforations may be hidden in this region.

Extensive damage to the small bowel or its mesentery may necessitate resection of a large segment of the bowel but anastomosis should always be performed.

The wounds of the colon are different because of the solid contents, the thin wall and the bacterial flora. Fresh wounds, especially stab wounds, may often be closed primarily in the transverse and right colon. Wounds with large areas of devitalized tissue and wounds in the lowest reaches of the colon require exteriorization or proximal colostomy with drainage. It is probable that all wounds of the colon which have been present more than six hours should be treated in this manner [*7*]. Perforations into the mesentery may occur from enema and irrigation tubes and are particularly bothersome. These should always be exteriorized or have a proximal colostomy performed as secure closure is difficult to accomplish.

Two of our five patients with wounds of the stomach died. One of these injuries occurred in the era before antibiotics were available. The patient died of septicemia due to Escherichia coli. The other patient was a premature baby with a huge perforation from a gavage tube, who died twenty hours after surgery with persistent signs of peritonitis.

Two patients with blunt injuries to the duodenum survived. One experienced a stormy postoperative course and complications from a duodenal fistula.

Two of eight patients with injuries to the small bowel died. One had carcinomatosis and died of peritonitis following plication of a perforation which had been caused by a trocar. The other was seen forty-eight hours after rupture of the ileum from blunt trauma and died of persistent generalized peritonitis eighteen hours after operation.

Two of fourteen patients with trauma to the large bowel died. One was a premature baby. The other was a sixty-three year old man who died from massive esophageal bleeding following resection and exteriorization of the colon.

Five of the survivors developed severe infection of the wound. Three of these had been treated by exteriorization or proximal colostomy.

The mortality in the group of patients with trauma to the hollow viscera resulting in perforation was thus a little less than 20 per cent.

COMMENTS

The diagnosis and decision whether to explore or not in abdominal trauma has to be arrived at almost solely by clinical means. If we review the number of positive laboratory findings or single findings which made exploration imperative or advisable, radiography was found most helpful. Four times it showed free air under the diaphragm, and once a free fluid level was seen on a lateral decubitus film.

Estimates of hemoglobin and hematocrit values were considered to have been of assistance twice in suspecting intraperitoneal bleed-

ing, but in both cases only thirty and forty hours after the injury occurred.

Leukocytosis has been mentioned as an early sign in rupture or injuries of the liver and the spleen caused by blunt force [*15*]. In this series only seven of fourteen (50 per cent) had an initial leukocytosis of 15,000 per cu. mm. or more.

The combined mortality was 22 per cent; somewhat less than 20 per cent among patients with injury to the hollow viscera, 38 per cent among those with hepatic and biliary injuries, 10 per cent among patients with injury to the spleen, and somewhat more than 10 per cent in the group in which exploration did not reveal penetrating lesions of the solid or hollow viscera.

The most common causes of death were massive bleeding from liver wounds and peritonitis from lesions of the hollow viscera. One death occurred in the group in which no open lesions of the solid or hollow viscera were encountered, but exploration was performed on the basis of our belief that, as a rule, exploration is imperative in wounds that penetrate the abdominal cavity even in the absence of signs of blood loss or peritonitis.

This death, which occurred from pneumonia in a sixty-one year old man, was attributed to this policy of aggressive intervention which we still believe is bound to be profitable in the long run.

One-third of the injuries in this series were caused by blunt trauma and two-thirds by penetrating trauma.

The interval between injury and operation could be accurately estimated in thirty-one of our cases of penetrating trauma and the average was 2.4 hours. On the other hand this time interval was over thirty hours for fourteen cases with blunt trauma. We believe this is one of the reasons for the higher mortality in the group with blunt trauma which in our series was 29 per cent versus 18 per cent for the patient with penetrating trauma, including injuries which occurred in the hospital.

It is of interest that the mortality among the group who sustained injuries in the hospital was very high. Five of eight patients in this category (62 per cent) died from their injuries. The explanation is found in the condition of these patients before the injury rather than the injury itself. Two were premature infants, two had carcinoma and the fifth was an elderly lady with a large, unrecognized intrahepatic hematoma.

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Solitary Schwannoma of the Small Intestine

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BENIGN tumors of the small bowel are quite rare. They are usually small, asymptomatic and discovered at autopsy. In 1932, Morrison [*13*] found only thirteen such tumors among 13,130 consecutive autopsies. Most of these tumors are fibromas or other neoplasms of connective tissue origin, while those of neurogenic origin are rare. In 1956 River *et al.* [*16*] reviewed the world literature which included reports of 1,399 benign tumors of the small bowel that were removed at operation. They found only ninety (6 per cent) of neurogenic origin of all histologic types including both ganglionic and supportive tissue cells. We recently observed a patient who sought medical attention for chronic hemorrhage for many months before a diagnosis was established. The history of this patient is presented herein together with a review of the world literature.

CASE REPORT

M. B., a fifty-six year old white housewife, was first seen at the University of Missouri Medical Center on August 11, 1958. Her chief complaint was "black tarry stools" of five days duration. These had first occurred two years previously with several episodes in the intervening period. These episodes were accompanied by vague epigastric pain unrelated to intake, but relieved by milk. There was no history of gross rectal bleeding, nausea, vomiting or hematemesis. In the previous two years she had been hospitalized elsewhere with the same complaints. Treatment there was confined to transfusion of 5 units of whole blood and an ulcer regimen. X-ray studies were reported as negative. In addition, she had been hypertensive for several years. Otherwise, the past history was noncontributory.

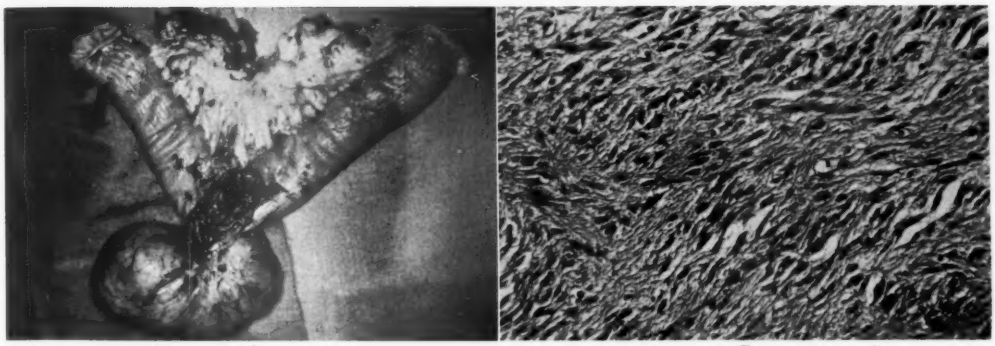
Physical examination revealed an obese, pale woman who appeared chronically ill. The blood pressure was 212/144 mm. Hg. The abdomen was tender in the epigastric region and right upper and lower quadrants but no masses were palpable. The remainder of the physical examination was negative except for mild arteriosclerotic retinopathy. A gastric aspirate was negative for occult blood to guaiac. Gastroscopy revealed that the gastric mucosa appeared to be normal without evidence of irritation, bleeding or neoplasm.

The laboratory results were as follows: hemoglobin, 9.5 gm per cent; hemotocrit, 29 per cent; and leukocyte count, 4,000 per cu. mm. with a normal differential. X-ray contrast studies revealed a hiatus hernia of moderate size; the small bowel series and barium enema were negative. Bleeding and clotting times and liver function studies were within normal limits.

A diagnosis was made of "sliding hiatus hernia with hemorrhage." She was treated with transfusion of 6 units of whole blood and an ulcer regimen. No bleeding occurred and she was discharged on August 30, 1958.

On December 5, 1958, the patient was readmitted after further episodes of melena. The hemoglobin was 5.5 gm. per cent and transfusion of 12 units of blood was required to maintain a hemoglobin level of 10 gm. per cent. A repeat contrast study of the stomach and duodenum was again negative except for the hiatus hernia, and gastric aspirate was negative to guaiac. The patient was transferred to the surgical service for repair of the hernia. Because of the patient's obesity, this repair was performed through a left posterolateral thoracotomy incision and the upper abdomen was explored through an incision in the diaphragm. Her convalescence was uncomplicated except for a small hemothorax which cleared rapidly after aspiration. No further bleeding occurred and the patient was discharged.

On January 24, 1959, she was readmitted for the third time with a history of further bouts of melena, and the hemoblogin level was 5.5 mg. per cent. Repeated x-ray contrast studies were again negative and demonstrated adequate repair of the hernia. Bleeding did not occur in the hospital. She was given 4 units of blood and discharged with instructions to return to the hospital immediately upon the first sign of melena. On April 17, 1959, she was readmitted in mild shock (hemoglobin 4.5 mg. per cent) and, after transfusion, underwent laparotomy the next morning at which time the tumor



A B

FIG 1. A, photograph of the tumor removed at operation; the jejunum was opened *in situ*. B, photomicrograph of the same specimen; note the tendency to pallisade. Original magnification × 120.

shown in Figure 1A was discovered in the lower jejunum. On opening the gut *in situ*, immediately over the tumor pedicle, a small funnel-shaped passage could be seen to extend into the stalk from which blood welled up as fast as it could be suctioned out. The tumor was resected along with 10 inches of jejunum and a wedge-shaped piece of mesentery. A primary end to end anastomosis was performed. One week postoperatively the course was complicated by the development of symptoms suggesting biliary colic but these rapidly disappeared. The patient was discharged on May 3, 1959. Follow up in the Outpatient Clinic one month later revealed that the patient was free of her former symptoms and without melena since operation.

PATHOLOGIC FINDINGS

Gross Description. The specimen consisted of a 21.2 cm. segment of jejunum with mesentery. (Fig. 1A.) A pedunculated nodule measuring 6.8 cm. in diameter was attached to the antimesenteric border. On section it was moderately firm, yellowish-grey with focal areas of hemorrhage and a central area of soft yellow tissue. The soft area was 1.5 cm. in diameter. There was a crater-like depression in the mucosa at the point of attachment. It was 0.3 cm. in diameter and 0.2 cm. deep, and it did not extend into the stalk.

Microscopic. A specimen from the main tumor mass consisted of interlacing bundles of spindle shaped cells which in some places have a tendency to form Verocay bodies. (Fig. 1B.) These bodies consisted of an island of fibers with the cells arranged in pallisading fashion at the periphery. There was extensive necrosis in one area.

Diagnosis. The diagnosis was: "pednuculated schwannoma of the jejunum with ulceration."

COMMENTS

There is much confusion in the older literature concerning the origin and nomenclature of tumors of the peripheral nerve sheath. The neurofibroma was first recognized as an entity by Verocay in 1910 and effort has been directed toward separating these and tumors of similar origin since that time, notably in the works of Penfield [*15*], Masson [*12*], and Stout [*17*]. There are two theories concerning the origin of these tumors. One is that they arise from fibroblasts of the mesoderm, and the other is that they originate from the Schwann cells and are of ectodermal origin. Current tumor nomenclature recognizes the entities of neurofibroma and schwannoma, but it is recognized that these tumors are often not of clear cut histologic types but occur as intergrades and mixed cell types. In addition both types of tumors have been observed to exhibit varying grades of malignancy or malignant degeneration.

Visceral neurofibroma and schwannoma occasionally appear as a part of generalized neurofibromatosis as originally described by von Recklinghausen in 1882 and have been reported from time to time. However, these ordinarily do not represent a diagnostic problem clinically since they are asymptomatic and found at autopsy or are recognized from the external clinical evidence of the disease. Isolated benign and malignant visceral tumors of the peripheral nerve sheath may also occur without evidence of generalized disease. Lindenmeyer [*11*] stresses their origin from the myenteric plexus, while Feyrter [*8*] divides them into two groups with origins from either the myenteric or Meissner's plexi.

The world literature was reviewed to study all cases of tumors of the peripheral nerve sheath in the small intestine. The great majority

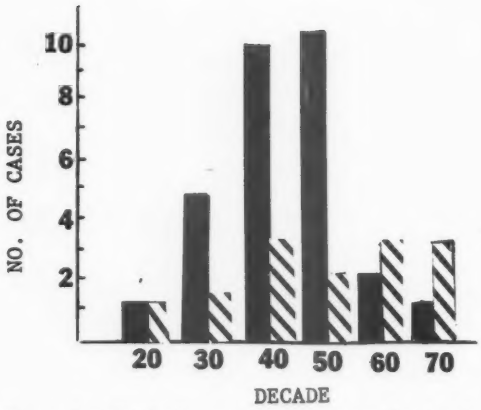


FIG. 2. Age distribution and number of cases by decade (forty cases). Lined columns indicate malignant lesions; black columns indicate benign ones.

of these were found in the European literature under a profuse number of descriptive terms. In many cases it was impossible to place the given tumor under the current classification of neurofibroma or schwannoma because of insufficient histologic information. Therefore, they were tabulated without regard to this classification and only with regard to their malignancy. The most complete review prior to 1939 is that of Collins [*4*], while Ekdahl [*7*] and Cedermark [*3*] summarized the Scandinavian literature. More recently Nilsson [*14*] tabulated several new cases in the European literature to which we add the cases of Forban [*9*], Dietrich [*6*], Kastrup [*10*], and the case reported by Nilsson.

A total of forty-five tumors were found and thirteen were malignant. In addition Nilsson mentions six other cases, one of which was malignant. References were not available for these (Bourgeon, Gaudin, Gronbeck, Schmidt, Berthon and Ungerstedt) and they are omitted from the tabulation.

Clinical. The age distribution is given by decades in Figure 2. For the benign tumors there is a decided peak during the fourth and fifth decades, while the malignant varieties occurred rather uniformly throughout the period from ages forty-five and up. The minimum age was twenty-nine years and the maximum seventy-three. There was no sex prevalence (nineteen females and twenty-one males). Both of these figures are from data on forty of the forty-five cases.

The presenting symptoms among the forty-five patients were as follows: hemorrhage, 23; pain, 21; mass, 14; obstruction, 5; diarrhea, 4; peritonitis, 4. These are listed according to the number of times cited. It is noteworthy that over half of the cases presented as chronic, intermittent upper gastrointestinal hemorrhage with melena, anemia and weakness. Three were anemic to the point of shock and required more than forty transfusions each. These symptoms persisted from one to fifteen years before diagnosis was established and the average delay before operation was around three years. The common past history was one of multiple hospitalizations over several years before laparotomy was performed.

Half (twenty-one) of the patients also had abdominal pain but did not give any uniform diagnostic value. This pain was often intermittent and vague in character, varying from mild epigastric discomfort to that mimicking ulcer, acute appendicitis or peritonitis. The painful area was not significant in determining the anatomic location of the tumor. Similarly, though fourteen cases presented with a palpable mass, this was usually discerned just prior to operation. The diagnosis of an abdominal mass was vague and seen in retrospect after several years of intermittent hemorrhage. It was not a diagnostic sign for which operation was performed.

Nine of these patients first sought medical attention because of complications due to the tumors. Five patients had bowel obstructions and four had perforation and peritonitis. Those with pain or a palpable mass are included among these cases. Four had the additional symptom of intermittent diarrhea. Most of the cases had been diagnosed and treated previously as peptic ulcer or chronic gastritis although four were diagnosed as acute appendicitis and two as pernicious anemia. The diagnosis of small bowel tumor was not made preoperatively in any case. In addition many of the patients had had x-ray contrast studies reported as normal and Botsford and Seibel [*1*] have adequately pointed out the difficulty in visualizing small bowel tumors on roentgenograms.

Two patients with malignant tumors presented with weight loss in addition to the symptoms of their counterparts with benign disease, but there was no consistent clinical pattern to separate the two. At operation two of these had metastases to the liver and six had extensive

local infiltrations so that their malignant character was not in doubt, but two other cases appeared grossly benign with local areas of malignancy. The longest survival after operation was four years, but it must be mentioned that most of these cases were found too late for an adequate radical operation and three recent cases (after 1950) do not include follow up, so that the survival time in no way indicates prognosis with current treatment methods.

Gross Appearance. The locations of both benign and malignant tumors were as follows: ten were duodenal, four jejunal, seven ileal and twenty-four unspecified ileojejunal. There is a great variety of anatomic types in relation to the gut wall which can roughly be divided into three groups: submucosal, intramuscularis, and subserosal. The first two types are described as bulging into the lumen of the intestine or annular in nature and produce early obstruction, while the latter and most common type is pedunculated and ranges in size from 1 cm. to 20 cm. in diameter. They are most frequently found at the antimesenteric border. While the exact origin cannot be identified with any certainty, it seems reasonable to assume that the submucosal and perhaps the intramuscular type originate from Meissner's plexus, while the subserosal types arise from the myenteric plexus of Auerbach.

They are described as smooth and firm, yellow to gray on cut surface and often with focal areas of degeneration, but both giant cystic and polypoid varieties have been observed. In one case (Boucheron [2]) of a malignant variety there was no indication of malignancy from the gross appearance. Boucheron advocated radical operation for all such tumors in view of the high incidence of malignancy (30 per cent in this series). We cannot agree with this since most tumors of the small bowel are benign fibromas rather than of neurogenic origin. The neurogenic tumors are diagnosed, only in retrospect, by the pathologist. The vast majority of these very rare tumors which were malignant are quite obviously sarcomatous on gross appearance. The frozen section can still be used in cases with excessive necroses or cystic change in the same manner in which it is used to examine uterine fibromas.

Histology: These tumors are divided into two types by the same criteria employed for nerve sheath tumors elsewhere. These are the schwannoma and the neurofibroma. However, the malignant variety is still of questionable classification and most frequently referred to as malignant schwannoma. At least some evidence is present which suggests malignant degeneration in a benign tumor as well as primary types. As indicated above, many of the case reports do not contain adequate histologic descriptions and occur under a diffuse terminology, while some that were considered to be neurofibromas are quite clearly schwannomas under current criteria so that an accurate division cannot be made. It is apparent, however, that the schwannoma is far more common.

Therapy. Local resection with restoration of the bowel continuity is the treatment of choice. There have been no recurrences of benign tumors to date. The presence of grossly malignant tumor or palpable regional nodes with a positive frozen section, would necessitate standard radical procedures, but we have not encountered a case of this nature. The indications for exploration are the presence of upper gastrointestinal hemorrhage evidenced by melena of uncertain etiology. These patients present a variety of gastrointestinal symptoms and are frequently thought to have one of the more commonly occurring diseases, but they continue to have melena in spite of conservative measures. One must not be misled by the absence of a palpable mass or the failure to demonstrate a tumor by radiographic means. We believe that a provisional diagnosis of small bowel tumor should be made in the presence of frank melena when other causes for the bleeding cannot be established with certainty, and the patient should be subjected to surgical exploration as soon as general conditions allow, depending upon the severity of hemorrhage.

SUMMARY

A case of isolated jejunal schwannoma is presented along with a review of the world literature about small bowel tumors of peripheral nerve sheath origin. Forty-five cases have been described in addition to six others noted but not included in the tabulation because of inadequate data. Of these cases, thirteen (30 per cent) were malignant. The clinical picture is discussed and over half of the patients are described as first seeking aid for massive upper gastrointestinal hemorrhage over periods up to fifteen years. Nonspecific pain, palpable mass and obstruction appear less frequently. The

gross and histologic appearance of these tumors is described, and the problem of malignancy is reviewed briefly.

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Effects of Cortisone on the Healing of Disrupted Abdominal Wounds

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THERE is a widespread clinical impression among surgeons that disrupted abdominal wounds heal with greater strength than primary wounds. Sandblom's work [6] furnishes experimental evidence to support this impression. He showed that secondary wounds tended to heal faster and with greater strength than primary wounds, even when the secondary wounds were made at some distance from the primary. Cortisone is generally considered to inhibit primary wound healing and to delay the formation of granulation tissue [1–5]. We are not aware of any studies regarding possible effects of cortisone specifically on the healing of secondary or disrupted wounds. Our interest in this problem was aroused by certain patients who developed disrupted abdominal wounds while on cortisone therapy.

MATERIALS AND METHODS

Rabbits weighing approximately 1.75 to 2.0 kg. were used as experimental animals. All procedures were performed under sodium pentobarbital and ether anesthesia, and a common commercial brand of hydrocortisone was given intramuscularly. Midline wounds 5 cm. in length were made through all layers of the abdominal wall, and closure was accomplished with continuous cotton suture placed through all layers of the abdominal wall. Wound strength was determined by a modification of the method of Meadows and Prudden which is essentially as follows: after removal of the sutures, a small abdominal puncture wound was made and a cannula with an attached balloon inserted into the peritoneal cavity in such a way as to place the balloon directly beneath the incision to be tested. The cannula was then connected to a mercury manometer and a forced air source, and the balloon was gradually inflated at a constant rate until the wound disrupted. The manometric pressure in millimeters of mercury was recorded at the moment of disruption.

The animals were divided into four experimental groups, each of which acted as its own control.

Group I, which consisted of twelve animals, served as a general control and did not receive cortisone. After five days the primary wounds were disrupted and resutured. Five days later the resutured wounds were similarly disrupted. This sequence of events was used in all groups, the only variable factor being the cortisone administration.

In Group II, which consisted of seven animals, the primary wounds were disrupted on the fifth day and resutured. Cortisone (25 mg.) was administered on the day of disruption of the primary wound and continued daily for five days; then disruption of the resutured wound was performed.

In Group III, which consisted of eight animals, 25 mg. of cortisone were given daily beginning on the day the primary wound was made and continued until the disruption of the secondary, resutured wound ten days later.

Group IV consisted of eighteen rabbits which were given cortisone (25 mg. daily) beginning five days before the making of the primary wound and then continued to the disruption of the resutured wound fifteen days later.

There were several animals who developed severe wound infections and eviscerated spontaneously when their sutures were removed. These animals were excluded from the study.

TABLE I
WOUND PRESSURES IN EXPERIMENTAL RABBITS*

No. of Animal	Initial Pressure (mm. Hg)	Second Pressure (mm. Hg)
2-6	77	156
2-7	74	144
3-6	50	200
3-7	100	160
3-8	140	140
5-11	42	88
5-13	56	108
5-14	64	166
6-11	62	156
6-12	74	166
6-13	44	230
6-15	48	200
Average	69.3	159.5

* Pressures are those at which the wound of the control animals disrupted (no cortisone).

RESULTS

Group I served as a general control for the animals treated with cortisone and also demonstrated the differences between primary wound strength and disrupted wound strength in normal rabbits. The pressure required to disrupt the initial or primary wound averaged 69 mm. Hg while the pressure required to disrupt the resutured (previously disrupted) wound averaged 159 mm. Hg. This represented an increase in wound strength of 131 per cent as determined by this method. (Table I.)

In Group II the average disruption pressure of the initial or primary wound was 120 mm. Hg, and the average disruption pressure of the resutured wound was 203 mm. Hg. This represented a 59 per cent increase in wound strength of the resutured disrupted wound over the primary wound. (Table II.)

In Group III the average disruption pressure for the primary wound was 84 mm. Hg, and in the resutured disrupted wound it was 102 mm. Hg. This represented a 21 per cent increase in wound strength. (Table III.)

In Group IV the average disruption pressure for the primary wounds was 59 mm. Hg, and for the resutured disrupted wounds it was 61

TABLE II
PRESSURES AT WHICH WOUNDS DISRUPTED IN GROUP II

No. of Animal	Initial Strength (mm. Hg)	Second Pressure (mm. Hg)
2-1	92	142
2-2	105	240
2-3	130	245
2-4	114	201
2-5	120	240
2-6	146	236
2-7	137	120
Average	120.5	203.4

TABLE III
PRESSURES AT WHICH WOUNDS DISRUPTED IN GROUP III

No. of Animal	Initial Strength (mm. Hg)	Second Pressure (mm. Hg)
1-1	84	116
1-2	50	98
1-3	85	94
1-4	94	106
1-5	105	108
1-6	70	112
1-7	112	80
1-8	72	102
Average	84.0	102.0

TABLE IV
PRESSURES AT WHICH THE WOUNDS DISRUPTED IN GROUP IV

No. of Animal	Initial Strength (mm. Hg)	Second Pressure (mm. Hg)
2-2	58	74
3-1	68	62
2-3	80	92
2-4	60	56
4-4	70	78
4-6	77	72
5-2	68	60
5-4	54	64
5-5	60	60
5-6	60	44
6-1	76	36
6-3	42	64
6-4	48	62
6-6	52	56
6-7	48	68
6-8	44	44
6-9	58	60
6-10	46	46
Average	59.4	61.0

mm. Hg. There was essentially no difference in the strength of the primary and resutured wounds in these animals who were on cortisone for a total of fifteen days. (Table IV.)

COMMENTS

The results of this study strongly support the concept of increased strength in disrupted resutured abdominal wounds compared to primary wounds. The results also show that the strength of resutured, previously disrupted abdominal wounds is definitely decreased by the administration of cortisone. The amount of decrease in wound strength appears to be in direct proportion to the duration of time on cortisone medication. This decrease in secondary wound strength may also be related to the size of the cortisone dose as well as to time; however, this feature was not explored in these experiments. It is also of interest that according to the conditions of this study cortisone had relatively little effect on the strength of the primary wound. This is evident if one compares the primary wound data in Group I with the corresponding data in Group IV in which the animals had been given cortisone for ten days prior to the disruption of the primary wounds. (Tables I and IV.)

Some physicians believe that increased vascularity and other local factors present in secondary wounds adequately explain the increased strength. However, Sandblom's work [6], in which he noted increased strength in secondary wounds which were placed at some distance from the primary wounds, suggests that some humoral mechanism may be involved.

The inhibiting effect of cortisone on the healing strength of disrupted, resutured abdominal wounds assumes clinical importance, because it is sometimes necessary to perform major abdominal operative procedures on patients who have been on cortisone for long periods of time. If the results of this study are at all transferable to human beings, it would appear that the resuturing of disrupted abdominal wounds in patients who had been given cortisone for extended periods of time would have no greater chance of success than did the primary wound closure.

SUMMARY

1. Disrupted abdominal wounds in rabbits heal with greater strength than do primary wounds.

2. Cortisone significantly decreases the strength of disrupted resutured abdominal wounds in rabbits.

3. The decrease in strength of the secondary disrupted wound appears to be directly related to the length of time of cortisone administration.

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Hemagglutinative Vaso-Occlusion in the Pathodynamics of Keloid

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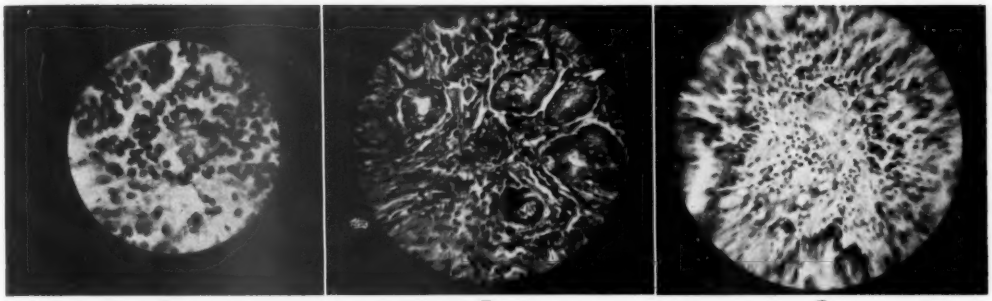
MANY years of observation on subjects with progressive or recurrent keloids has led to awareness of the complicated emotional and surgical problem presented by these lesions. In spite of the recent advocacy of steroid and enzymatic approaches to their treatment, the unsatisfactory solution of relentless and repeated excision has proved to be the only really positive one. During this period of observation, there has been the impression that these lesions in most subjects are not uniformly progressive. Practically all keloids show rather accelerative or decelerative growth changes as well as unpredictable "flares" at restricted portions of their peripheries. Contrary to what one gleans from the literature, these changes are overtly inflammatory in character.

Within the past six years, histologic studies of excised keloids have been extended to more detailed examination of those areas (as well as to other lesions proving to have similar pathodynamics) of keloids exhibiting pleomorphic changes at the margins contrasting with the relatively static situation extant in the body of the lesion. These studies coincided in time with another investigation dealing with the dynamics of "static ulcers." To our surprise the histologic findings in the margin of many keloids was so similar to those in the margins of either varicose, decubitus, or even gastric and intestinal ulcers, that selected microscopic fields of either of these apparently grossly dissimilar lesions could not be distinguished insofar as the character of the contributing vaso-occlusion was concerned. Since the study of "static ulcers" had yielded a profitably working hypothesis of their genesis and establishment, this hypothesis seemed reasonably extendable to the genesis of keloid [1].

To facilitate that extension our theory of the pathodynamics of "static" dermal ulceration will be briefly reviewed and amplified. We had found that the marginal capillaries and venules of dermal ulcers were plugged with nonfibrinous thrombi consisting of agglutinated erythrocytes. The pattern of this intravascular hemagglutination was identical to that which could be produced by the interaction of red blood cells with various partially depolymerized mucopolysaccharides. The presence of such mucopolysaccharides in wounds has been demonstrated repeatedly [3,4]. These depolymers appear in soluble, diffusible form (thus being able to enter the capillary lumen to cause hemagglutination) from either of two sources; (1) during the process of polymerization by which new "ground substance" is being built up by mast cells or other sources of polymerizing enzymes, and (2) as a stage in the decomposition of established ground substances (reticulin, hyaluronic acid and collagen) by the mucodepolymerases (such as hyaluronidases) present in wounds. In fact, the actual concentration of these transition forms of mucopolysaccharide which are most capable of causing capillary blockage through their hemagglutinative effect has been shown by Sylven [2] to be a function of the degree of dynamism of the wound. Because of high concentration of median molecular polymers in varicose and decubitus ulcers, which reflected the same dynamism our histologic studies on them had suggested, we disavowed the term "static" for these lesions [1].

Concurrent with the observations about keloid and stasis ulcer, certain general observa-



A B C

FIG. 1. A, occluded blood vessel (center) in advancing margin of keloid. The occlusion is not complete in the fixed specimen because of sickle trait in this subject. The sickling occurs after excision. There is marked lymphocytic infiltration and beginning transformation of perivascular lymphocytes into fibroblasts. B, pseudoacinus (center) in a granulomatous peptic ulcer. While superficially resembling a mucus gland, the interior of this structure consists of compacted spherocytes. A patent blood vessel is seen at five o'clock. The relative absence of mast cells in this granulation tissue, contrasting with the relative plentitude of such cells in the submucosa of the gastrointestinal tract may be significant. C, hemagglutinative, nonfibrinous thrombi (center) in an advancing squamous cell carcinoma.

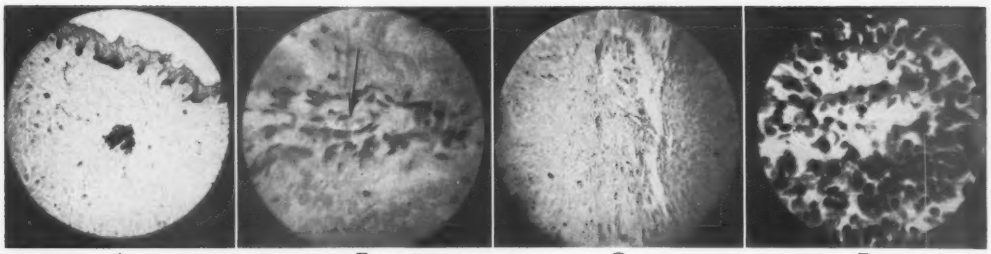
tions had led to conclusions about the significance of these median molecular weight mucopolysaccharides in regard to their local action in causing hemagglutination in various sites such as keloid (Fig. 1A), peptic ulcer (Fig. 1B), or even in overt carcinomas. (Fig. 1C.) These observations are not novel. Knisely and his coworkers [*13*] have invoked an etiologic connection between an *in vivo* phenomenon which they termed sludging (this *in vitro* phenomenon had been earlier described as pseudoagglutination [*5*]) and a variety of clinical conditions, but the discovery of this phenomenon as associated with keloid suggested that enhanced autohemagglutinability in this connection might be attributed to certain constitutional predisposition or "diathesis" factors. Bloom [*11*] has given an excellent review of the literature pointing to the familial or hereditary tendency to keloid and has recognized that keloid and peptic ulcer might have a commonly underlying systemic basis. However, blood group studies by Bloom and Levine were made on too small a series to have significance from this standpoint. Although our series is much larger (seventy cases), it is still too small for statistical blood group analysis. However, we can say that our group (entirely Negro) does have a determinative blood group characteristic which will be elaborated in another portion of this report.

MATERIAL

In most instances the histologic material studied was from fully excised initial or recurrent keloids obtained from the surgical service. In some instances only that portion of the margin which exhibited the inflammatory "flare" previously mentioned was removed for biopsy. Standard histologic preparation and staining were used but the histologic examination consisted of attention to cytologic detail as seen under oil immersion magnification.*

One hundred thirty-three excised keloids or biopsy segments removed from keloids left *in situ* were examined histologically. While some of these examined lesions had been treated with cortisone, hyaluronidase infusion and irradiation, they were for the most part "native" or untreated keloids removed for cosmetic reasons. In all but two instances the removal or the biopsy had been performed after anesthesia

* While ordinary "high dry" examination, or even low power will bring out all the characteristics of the pathodynamic sequence as outlined herein, much time was devoted to the cytology of the keloid flare area and an attempt to determine the mast cell population of that area. This was the case because it was believed that a mastocytosis in any area will prevent the type of intracapillary hemagglutination leading to keloid. While not strictly germane to the present thesis, the mast cell is becoming increasingly recognized as the mediator of normal connective tissue replenishment, and this point is made because a theory of systemic enzyme therapy (as has occasionally been applied to treatment of keloid) is that such administered enzymes cause a discharge of heparinoids from mast cells. These heparinoids act as anti-inflammatory and anti-hemagglutinative agents [*12*]. They would, if present in the keloid area, tend to limit its progression. It is our present impression that the mast cell concentration in keloid scars appears to be considerably lower than in other collagenizing tissues.



A B C D

FIG. 2. A, periphery of proliferating keloid removed during the flare stage. Note markedly dilated lymphatics and hemagglutinatively occluded blood vessels (black material in the center is an artefact for marking the area desired for photographing). B, fibroblastosis adjacent to a longitudinally sectioned, hemagglutinatively blocked capillary. C, low power magnification of flare region of active margin of a keloid showing marked lymphangectasia. This appearance has led to the term lymphangiofibroma for keloids of this type. On this basis such keloids can be made to disappear or shrink by continuously applied pressure [6]. D, free sickle cells in nonthrombosed vascular basis at the margin of a keloid. Although this area is relatively cellular (as is common to the border of keloids), the relative lack of fibroplastic transformation suggests that this margin is not in a proliferative state.

with infiltration of procain. The two patients who had their keloids removed under cyclopropane anesthesia consented to the general anesthesia at our request. When we discussed the marked lymphangiectasia of some keloids, pathologists had raised the question of possible induction of the latter by pressure of injected procaine. The presence of dilated lymphatics in keloids removed under general anesthesia answers this criticism.

HISTOLOGIC OBSERVATIONS

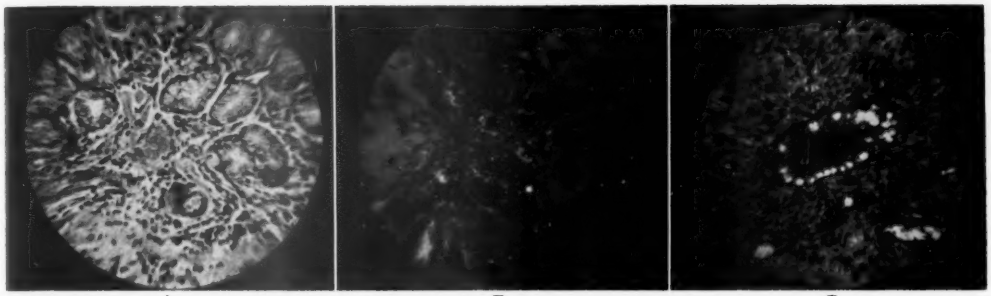
The majority of keloids examined showed the classic picture of anastomosing strands of hyalin collagenized matrix with numerous fibroblasts. Figures 2A and B show this picture and the plugging of all blood vessels with hemagglutinative thrombi. In the former figure the relatively hypoplastic epithelium with short rete pegs and slight cornification also can be seen. The intertrabecular lymph spaces are quite prominent and this is interpreted as a compensatory nutritive facility that has permitted retention and growth of epithelial elements.

In other instances, the enhanced lymphatic circulation takes the form of a lymphangeosis rather than an interstitial dilation of lymph spaces. This is shown in Figure 2C where the occluded vessel contains a sickle cell agglomerate.*

Although this type of red cell agglomeration may be determinative of keloid in some cases and while it furnishes a link in a chain of evidence forged to connect keloid with stasis ulcers (a frequent complication of frank sickle cell disease) such cells have been encountered in cellular margins of a keloid which showed no capillary thrombosis at the time of excision. (Fig. 2D.) It is instructive that this was a quiescent keloid.

In four instances serial biopsies of a flaring keloid margin after the spontaneous subsidence of the inflammatory flare were secured. This expedient permitted extension of observation of the vaso-occlusive sequence. While that type of occlusion leads to fibroblastosis and finally collagenized fibrosis (and thus causes the increment in the size of the lesion), evidence has been gathered that these thrombi undergo lysis and permit recanalization of the occluded blood vessel. Figure 3A is included because it shows an important phase in this recanalization. It was selected from a peptic ulcer granuloma for purposes of better illustration since such granulomas are more liberally vascularized than keloids. The characteristic "flat coin" pattern

* In this particular instance it is not possible to state that the sickling was postoperate and occurred in the interval between excision and formalin fixation since surgical specimens remain unfixed in the hospital until after the surgical pathologic description has been rendered. Oxygen tension diminishes in such excised tissue during that interval so that sickle trait becomes manifest in about 10 per cent of all specimens when the hospital population is predominantly Negro. However, the compactness of depicted thrombus suggests that it occurred before excision and that sicklocytosis may have been the actual vaso-occlusive instigator of this particular keloid. Strong evidence of sicklemia as the local ischemic factor which precipitates the development of gastric ulcers in Negroes is adduced from studies by Felix and his co-workers.



A B C

FIG. 3. A, hemagglutinative thrombus in granulation tissue from margin of a gastric ulcer. Partial recanalization at the margins is evident but the area is chosen to illustrate the flat coin pattern of the agglutinated erythrocytes as well as the spherocytosis exhibited. B, peripheral hypochromia (reversal of normal red cell appearance) in the involuting corpus hemorrhagicium. C, presumably mucoprotein induced spherocytosis and hemagglutinative thrombosis in a venule of ovarian stroma.

of the erythrocyte aggregate can be seen. Individual erythrocytes are also seen, and these evince a morphology in direct contrast to that of the usual, normal, biconcave red blood cells which exhibit a dark periphery and a relatively hypochromic center when seen in its full diameter. In the prehemolytic spherocytosis exhibited in Figure 3A the picture is the reverse. Each cell has a hypochromic ring around it instead of exhibiting a hypochromic center.

The role of partially depolymerized mucopolysaccharides in the production of this erythrocytic abnormality, which precludes the formation of rouleaux by which normal erythrocytes progress through capillary channels, will be recapitulated in another section. From an observational standpoint it is of interest that organs having a high mucin content, such as ovarian stroma (Fig. 3B) or corpus hemorrhagin (Fig. 3C), can normally exhibit the type of red cell agglomeration described in connection with keloid.

COMMENTS

Neither the ability of partially depolymerized mucopolysaccharides to cause pseudohemagglutination nor the idea that compensatory granulomatosis may follow vaso-occlusion and the tissue hypoxia entailed are original. The pseudohemagglutination (or sludging as it has been termed by others) within certain capillary beds has been described in a variety of lesions. It has even been reported systemically and the lymphangiectasia of keloids is so well documented that earlier authors designated many of them as lymphangiofibromas [6]. We cannot be certain that the hypothesis by which this lymphangectasia becomes contingent on the observed intracapillary hemagglutination is novel. The justification for the report extends beyond the restrictive material presented to the value of the hypothesis formulated. The merit of this hypothesis lies in the fact that it provides an explanation for the acknowledged racial predisposition to keloid.

The agglutinin which produces the nonfibrinous thrombi found in the margins of keloid and in indolent dermal ulcerations is a mucopolysaccharide or its protein combination, a mucoprotein [3]. In a local lesion it arises metabolically in the formation of the extracellular constituents of tissues; the ground substance, the reticulin, and the collagen. Any soluble mucoprotein of proper median molecular weight will agglutinate erythrocytes. Ordinarily, such median mucopolysaccharide derivatives are at a low concentration in tissues because they are being organized into insoluble (high polymer) ground substances of high molecular weight. A further component of this small amount of soluble (partially polymerized) mucopolysaccharide is in the process of transport from disintegrating or depolymerizing ground substance. The extracellular material of connective tissue is not "dead" or static but is constantly being degraded and replenished. The process is entirely analogous to that by which tissue proteins are continually being polymerized from amino acids and depolymerized, in turn, into them. In the case of ground substance, the building blocks are predominantly carbohydrate in constituency, but the analogy holds.

Depolymerized (solubilized) ground substance mucopolysaccharide has a sufficiently low molecular weight so that it can diffuse into the capillaries of the area in which it arises. This makes possible its entrance to the systemic circulation where it appears as transport mucopolysaccharide in combination with plasma globulins. Therefore, the local concentration of these mediomeric mucopolysaccharides is seldom sufficiently high to cause intravascular hemagglutination unless some combination of several conditions is present. First, there may be failure in transport of accumulated, disintegrated ground substance from the area because of a sluggish venous return. The last factor probably explains the vascular hemagglutination invariably encountered in the margins of varicose ulcers and the fact that these ulcers will frequently heal when simple expedients to improve the venous carriage are instituted. Secondly, the amount of transport mucopolysaccharide in the circulation may be elevated so that the circulation through an affected area is on the verge of having hemagglutinin already present in "transport" form, and they may initiate the sequence described above. It is unquestionably on this basis that dermal ulcers frequently occur in cryoglobulinemia or in various forms of hemolytic anemia in which a circulating "auto-antibody" (always a mucoprotein) is already present.

In truly cachexic subjects, as distinguished from those with simple inanition, this explanation for the propensity to decubitus also holds because there is invariably an increase in plasma mucopolysaccharide arising from generalized catabolism of ground substance in states like advanced cancer or collagen vascular disease. It must be understood that ground substance structures (which include substances such as ossein, chondrin, elastin and collagen) make up about 40 per cent of the body weight. This percentage of weight cannot be lost without reflection in the transport mucopolysaccharide on its way to elimination from the body. The hemagglutinating tendencies of the cachexic patient with cancer is probably expressed by intolerance to blood transfusion, but the general implications of mucopolysaccharide turnover, *systemically*, is left for further communication. Here we are interested only in local significance.

Third, there is the condition posed by the fact that different specimens of erythrocytes vary in their hemagglutinability. Anyone who has done crossmatching preparatory to transfusion is familiar with this variance. Some people's erythrocytes are easily agglutinable by low concentrations of mucopolysaccharide while others require high concentrations and in some instances (when there is a "blocking antibody" present) they may be quite inagglutinable. As a rule, subjects with Rh positive blood have erythrocytes that are more easily agglutinated than those of subjects with Rh negative blood, even by such a nonspecific hemagglutinin as porcine gastric mucin [7]. In sickle cell anemia or even in the presence of the trait, hemagglutinability may be so enhanced that it can occur spontaneously.

It could be more than coincidence that racial susceptibility to keloid parallels racial propensity for those factors which enhance erythrocyte agglutinibility. Both the susceptibility and the propensity are only heuristically acceptable at present from the clinical impression that there is this racial predisposition to keloid on a basis of empiric acknowledgment. Clinicians are aware of the fact that there is a higher incidence of keloid as well as a higher incidence of, for example, Rh positivity and sickle trait and relative hyperglobulinemia. These are parameters which tend to enhance the degree of autochthonous hemagglutinability among Negroes. Keloids and factors leading to hyperhemagglutinability (such as unusual hemoglobin types, sickle trait and hyperglobulinemia) occur in all races and an absolute correlation between them is a statistical rather than a clinical chore.

Our presented hypothesis cannot be elevated to the dignity of theory until there is a statistical demonstration that enhanced hemagglutinability triggers and maintains keloid proliferation. This does not necessarily abrogate the utility of the hypothesis since it can still predict new emergences. Thus, we can predict that a lowering of the median molecular weight mucopolysaccharide concentration in a dermal area below the level necessary for autochthonous hemagglutination would reduce either the tendency for keloid to occur or its rate of proliferation. It must be emphasized that the dynamic recurrence of the situation held responsible for the genesis of the lesion is part of the presented hypothesis. Other conditions remaining stationary, there would be two general methods available for limiting local accumulation of the particular aggregation of mucopolysaccharide held responsible for intracapillary hemagglutination. One of these methods would be by the addition to the system of a powerful inhibitor of depoly-

merizing enzymes, something which, for example, would combine with and maintain ground substances present in their fully polymerized insoluble form by antagonizing the action of hyaluronidase present. The corticosteroids (cortisone, hydrocortisone and prednisolone) are said to possess such noncompetitive antidepolymerases and there have been reports of their efficacy in keloids. A second method would be the administration of "competitive" antidepolymerases of the heparin class. Such inhibitors operate by posing a substrate-like structure to the enzyme; their application to stasis ulcers is known but that to keloid is only now under way.

A possible third method of approach to keloid therapy on the basis of preventing the hemagglutinative vaso-occlusion might be the application of depolymerizing enzymes. The theory behind this expedient (actually reduced to practice in the experimental application of hyaluronidase to keloids [9]) is that mucopolysaccharides would be completely degraded to low molecular weight sugars which are not hemagglutinative [8]. This explanation calls for a specific activity on the part of the depolymerizing enzyme which we now know is not the basis for their therapeutic activity. Enzymes are working chemically in an entirely different manner than was once thought to be operative [15,16]. It appears that *any* enzyme has a "semiconductor" chemical nature and can electrostatically discharge mast cells [17]. This property has now been demonstrated *in vivo*, not only for depolymerases but for such enzymes as anhydrases and oxidases as well [18]. Since the mast cell usually contains a large amount of heparin (the most powerful physiological competitive antidepolymerase known) which is liberated on discharge of these cells, whatever therapeutic efficacy resides in enzyme application may be explained on the basis of this release of such a competitive depolymerase inhibitor.

SUMMARY

A correlation of clinical and histologic observations on keloid has led to a hypothesis that local intracapillary hemagglutination produced by partially depolymerized ground substance in an area subject to trauma is involved in the genesis and maintenance of this lesion. Nutrition must be carried by dilated lymphatics because the reparative capillaries in the area are plugged. This nutrition is inadequate for normal repair but is adequate for recurring fibroblastic proliferation and a covering, hypotrophic epithelium.

The hypothesis is in keeping with the known predisposition to keloid of certain racial groups, which also have a high incidence of factors leading to autohemagglutination. It explains reported results in the clinical management of keloid by agents which reduce the concentration of hemagglutinative mucopolysaccharides in an involved area, such as cortisone or hyaluronidase.

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Surgical Repair of Patellar Fractures

COMPARATIVE ANALYSIS OF VARIOUS TECHNICS

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FRACTURES of the kneecap without separation of the fragments are usually comminuted stellate-like fratures; however, they may be transverse and often are longitudinal [*16*]. Surgical repair of these is seldom indicated. Immobilization for three or four weeks is usually all that is necessary and the results are almost uniformly good. If these fractures without separation are compounded and if the fracture is treated early enough, surgical debridement and suturing of the wound is indicated.

FIG. 1. Note marginal fracture which is a longitudinal one, not visible on the side view and not visible on the anterioposterior view. Insert shows how to make this film.

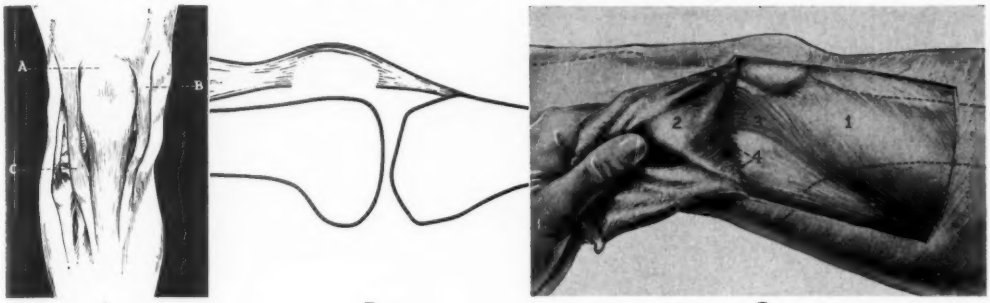
An anterioposterior roentgenogram should always be made through the kneecap with the knee acutely flexed in these fractures. Otherwise, longitudinal, marginal, depressed fragments may be missed. (Fig. 1.) These can usually be reduced by pressing the patella firmly against the smooth underlying femoral groove, placing a compression pad on it and immobilizing the knee for three or four weeks. (Fig. 10.) If compression will not reduce the fragment accurately, open reduction or removal of that marginal fragment should be performed. One should ascertain that the articular surfaces are smooth.

Transverse fractures of the patella with separation of the fragments always must be repaired surgically. The surgical technics that have been used in repairing patellar fractures may be divided into the following classifications: (1) operations in which only the bone is repaired, (2) operations in which only the torn soft tissue is repaired, (3) those in which the bone and the soft tissue are repaired, (4) operations in which the entire patella is removed, (5) operations in which part of the patella is removed, and (6) external fixation devices.

I shall discuss the advantages and disadvantages of these different operative procedures. These comments and opinions are based upon my personal experience in the treatment of 254 patients with fractures of the patella over a period of twenty-four years, a follow-up study of 216 of them [*14*], data secured from the literature on fractures of the patella and some data secured from a large Workman's Compensation Insurance Company.

ANATOMIC DETAILS

Before discussing and analyzing these various technics, two pertinent anatomic details of



A B C

FIG. 2. A, (a) central quadriceps tendon enveloping patella, (b) aponeurotic tendon of vastus medialis, (c), tendon of vastus lateralis. B, since the patella is strongly adherent to the central tendon, removal of the patella weakens the tendon. C, shows that fascia lata is a separate layer from tendons of vasti: (1) vastus medialis, (2) fascia lata, (3) tendon of vastus medialis, (4) blending line of fascia lata and retinaculum. (This drawing [C] was originally published in: EGGERS, G. W. N. Surgical division of the patella retinaculum to improve extension of the knee joint in cerebral spastic paralysis. *J. Bone & Joint Surg.*, 39A: 80, 1957.)

those structures around and about the patella should be noted. A detailed knowledge of these two points is obligatory if one attempts to repair patellar fractures successfully.

Anatomy of the Quadriceps Tendons. The quadriceps muscle is attached to the tibia by three tendons, not one. (Fig. 2A.) On the medial side there is the flat aponeurotic *tendon of the vastus medialis*. The *tendon of the vastus lateralis* is on the lateral side, and the main large tendon called the *central quadriceps tendon* is in the center.

The central quadriceps tendon is a single, large, strong tendon. It runs from the muscle above to the tibial tubercle below and the patella is encapsulated within its substance and strongly adherent to it. The patella is a sesamoid bone. The part of the central quadriceps tendon which lies over the front of the patella is called the *prepatellar portion*. On either side of the patella are thickenings of this central quadriceps tendon called *parapatellar thickenings*.

Significance: The kneecap can be removed completely from the central quadriceps tendon, but if that tendon is intact and if the downward expansions of the vasti are intact, the patient obviously will still have fairly strong extension power of the knee.

However, if a patella is removed completely or in part from the central quadriceps tendon, the midportion of that tendon is weakened structurally. The patella occupies an integral space within that tendon and is strongly adherent to it. Hence, removal of the kneecap weakens the central tendon at the place where it is removed. (Fig. 2B.)

If the central quadriceps tendon and kneecap is intact and strong but the flat tendons of the vasti are severed, the patient can still extend the knee completely straight. However, it is weaker in extension than if all three components are present. There is also some slight rotary instability in this extended position.

If the central quadriceps tendon is completely severed but the tendons of the vasti are intact, a person still can extend the knee while sitting on a table with the leg hanging down at a right angle to fully 45 degrees by the action of the tendons of the vasti.

Fascia Lata at the Knee Joint. The fascia lata on either side of the patella blends with and becomes a part of the patellar retinaculum and capsule at a level which is a little below the middle of the patella. (Fig. 2C.) Thus, if a transverse incision is made on either side of the kneecap at the level of the middle of the kneecap or above, one will incise skin, subcutaneous tissue, fascia lata, and then the downwardly extending aponeurotic tendons of the vasti and capsule. *Therefore, the fascia lata at the level of the middle of the kneecap is a separate layer.* It is separate and distinct from the flattened tendons of the vasti. It lies over and in front of them but is separate from them. In some instances the fascia lata blends with the patellar retinaculum at a little higher level, but not often.

Over the front of the knee the *thickened fibrous strands of the fascia lata curve inward*

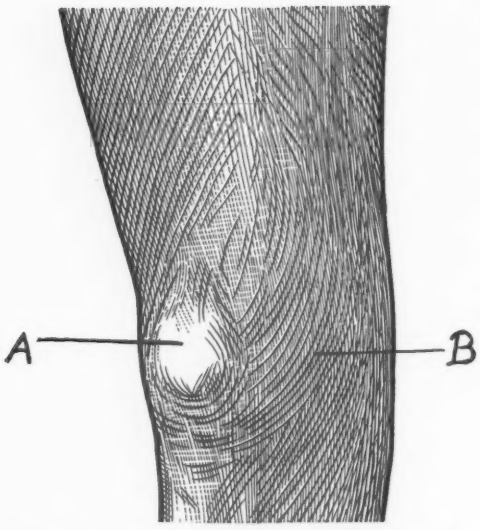


FIG. 3. (a) patella, and (b) fibrous strands of fascia lata curve toward the kneecap. (Redrawn from TOLDT, CARL. An Atlas of Human Anatomy, Fig. 1284, p. 848. New York, 1919. Rebman Co.)

toward the patella, instead of being arranged in a vertical direction. They are strengthened by arcuate fibers from adjacent muscles. (Fig. 3.)

Significance: Because the fascia lata is strengthened at the level of the knee with these oblique arcuate fibers it is not easily torn. Since these fibrous strands curve toward the patella, a vertical strain up and down the limb on these fibers often makes them stretch slightly apart in multiple small areas instead of rupturing transversely. Thus, *the fascia lata usually is not torn apart with its margins widely separated in transverse fractures of the patella.*

Since the fascia lata is a separate layer from the tendons of the vasti and is seldom ruptured in transverse separated fractures of the patella, *the operating surgeon may not see the torn separated tendons of the vasti because they lie underneath an intact and untorn layer of fascia lata.* (Fig. 4A.)

PATHOLOGY

In the usual type of transverse fracture of the patella, the bone is broken somewhat transversely. The upper and lower fragments are separated to varying degrees. There are usually more than two single fragments of bone. The kneecap is usually somewhat comminuted, although the upper and lower major fragments may appear to be solid in roentgenograms. Sometimes one or more small pieces of bone are broken entirely loose and may drop down into the knee joint.

In the average patellar fracture there is fairly

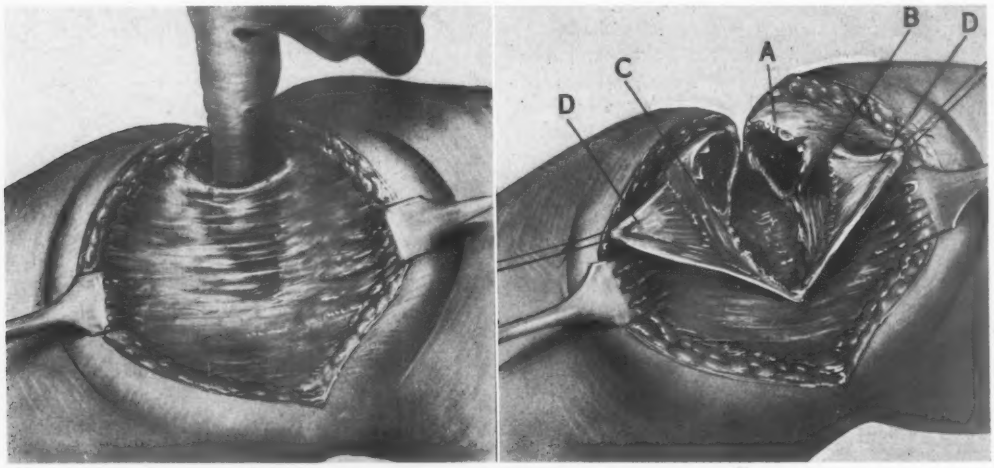


FIG. 4. A, finger is placed between separated patellar fragments. Note tear of vasti tendon beneath an intact and untorn layer of fascia lata. B, (a) complete rupture of prepatellar portion of central quadriceps tendon. Torn margins hang down over raw patellar surfaces, (b) torn parapatellar thickenings of central tendon, (c) torn vastus tendon, (d) fascia lata has been cut traversely and margins retracted up and down.

wide separation of the fragments (about an inch). A complete rupture of the prepatellar portion of the quadriceps tendon will be found. The torn margins will be shredded and will hang down over each of the broken, raw, bony surfaces of the patellar fragments. (Fig. 4B [a].) The parapatellar thickenings of the central quadriceps tendon will be torn apart and will be widely separated. (Fig. 4B [b].)

The flat tendons of the vastus medialis and vastus lateralis will be torn. The edges will be ragged and they will be widely separated, and the adjacent capsule of the knee joint will be torn. (Fig. 4B [c].)

The fascia lata on either side of the patella may appear to be swollen, contused, hemorrhagic, or stretched to some degree, *but as a rule it is not torn.* If it is torn at all, it is only torn about one-fourth of an inch on either side of the patella. (Fig. 4A.) If a transverse cut is made in this intact layer of the fascia lata at the level of the fracture and these portions are turned upward and downward exposing the downwardly extending aponeurotic tendons of the vastus medialis and vastus lateralis, one will find broad tears of these tendinous structures with wide separation. (Fig. 4B.) *These tears in the tendons of the vasti cannot be seen as a rule, unless the intact, overlying layer of fascia lata is cut and retracted to expose them.*

If there is extremely wide separation of the fragments (two or three inches), oblique or slightly curved short tears of the fascia lata on either side of the patella may be found in addition to the other tears and ruptures previously mentioned. However, this is found infrequently.

Sometimes the fascia lata is torn transversely about an inch or two below the tears of the tendons of the vasti. This occurs at the place where the fascia lata blends with the capsule. I have seen this only three times.[1]

When only a minimal degree of separation is present (not over one-fourth of an inch) the prepatellar portion of the central quadriceps tendon is torn and the parapatellar portions are partly torn but the vasti tendons are not torn. Sometimes the medial vastus tendon is torn but the lateral one is not. This is usually seen in knock-kneed people.

In those instances in which the fascia lata blends with the patella retinaculum and capsule at the level of the upper pole of the patella, there will be noted a stretching and relaxation of the combined fascia lata retinaculum capsule

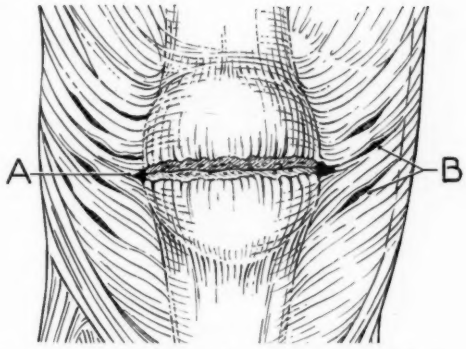


FIG. 5. (a) Marginal tearing of fascia lata at fracture site, and (b) multiple stretch tears in fascia lata.

tissues on either side. There will be multiple irregular stretch tears in it. In this type of stretch tearing there usually will not be much separation of the patellar fragments, regardless of the severity of the inciting injury. (Fig. 5.)

When only the lower pole of the patella is fractured, tearing of the vasti tendons is infrequent since this area is strengthened on each side by the fusion or blending of the fascia lata with the capsule and vasti tendons.

Significance. It seems obvious from this review of the pathology of patellar fractures that an accurate closed reduction of a separated transverse fracture of the patella is impossible. Those shreds of tissue which hang down between the fractured surfaces make it impossible for the patellar fragments to be replaced accurately in the proper anatomic position. (Fig. 4B [a].) Such a patella usually will heal with fibrous union and separation. Furthermore, it obviously is impossible to repair the ruptured tendons of the vasti by a closed reduction technic.

If the torn vasti tendons are not properly sutured, there obviously will be some weakness in extension of the knee regardless of how strong the central quadriceps tendon is and how well the patella heals.

If the central quadriceps tendon and the patella are properly repaired and heal strongly, solidly, and well, but the tendons of the vasti are not repaired, those margins of the vasti tendons which gap open will heal with a large mass of scar tissue between them. The scar tissue is adherent to the capsule behind and the fascia lata in front and effectively limits the regaining of flexion in the knee. (Fig. 6.)

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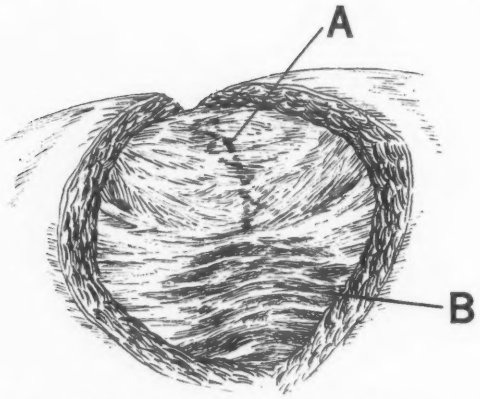

FIG. 6. (a) Healed fracture of patella, and (b) mass of scar tissue between open margins of vasti which is adherent to intact fascia lata, thus limiting flexion of knee.

If these torn tendinous vasti extensions are properly sutured along with the central quadriceps tendon, there will be a minimum formation of scar tissue between the ruptured margins of the vasti. The patient will regain motion more rapidly and more completely. Furthermore, full extension strength of the knee is assured.

If the lateral vasti tendons are properly closed and the parapatellar portions of the central quadriceps tendon are sutured snugly and tightly together, and if the superficial portion lying over the front of the kneecap is accurately closed, the fragments will automatically be replaced accurately in their proper anatomic position and its fresh bony surfaces are drawn accurately and snugly together.

OPERATIVE TECHNICS

External Fixation Devices. Several mechanical devices have been used in an attempt to hold the patellar fragments together without making an incision in the skin. Steinmann pins may be placed transversely through each of the major fragments of the patella and held together with rubber bands or wire. A four pronged claw-like device with a connecting screw may be used. Two of the prongs fit into the patella above the fracture and two fit into the fragment below the fracture line. When the screw is tightened, it pulls them together. Devices which clamp into the soft tissues above and below the patella and pull toward each other have been used. Adhesive tape has been used in an attempt to pull the patellar fragments together. All of these methods are doomed to failure because:

1. It is impossible to get the patellar fragments in close apposition because the fibers of the torn prepatellar portion of the central quadriceps tendon which hang down over the raw bony surfaces at the fracture line prevent the bone from coming closely together.

2. It is impossible to maintain the patellar fragments in exact anatomic alignment with these external fixation devices and insure smooth approximation and alignment of the articular surfaces.

3. It is impossible with external fixation devices to remove any loose pieces of bone which may have dropped down into the joint.

4. These methods cannot repair the torn aponeurotic tendons of the vastus medialis and vastus lateralis.

Removal of the Patella. The patella serves a useful purpose in the knee and it should not be removed because of a simple fracture. If it is badly damaged by disease, infection, degeneration, tumor growth, or possibly by extremely severe injury plus disease of the bone, removal of the patella may be indicated because the weakened knee which is left after removal of the patella may be a more functional knee than if the patella were left in place. However, an extremely high percentage of all fractures of the patella can and should be repaired surgically so that the bone can heal, since the patella does serve a useful purpose in the knee. There are many articles in the literature that attest to this.

Garber states [9]: "Total patellectomies should not be employed for all fractures of the patella. There is much evidence to support the contention that knee joint efficiency is reduced . . . ." He also describes the formation of calcified areas in the repair zone which may be irritating to the subjacent femoral groove.

Heineck [13] was apparently the first surgeon to practice total patellectomy, but he disapproved of the procedure because of the subsequent weakness in the knee.

De Nio and Hudson [5] emphasize: "The defect made by excision of the patella must be repaired with rectus tendon." They recognized that structural weakness of the extensor mechanism of the knee was present after the patella was removed and that this weakness must be repaired.

Crenshaw and Wilson [4] state that, "The patella serves a useful function and should be preserved in transverse fractures . . . ." They also state that, "Following patellectomy there is more tendency for residual instability and weakness than when . . . "

Rapp [20] states, "The loss of the patella weakens the quadriceps to some extent, detectable by dynamometric measurements."

Haxton [12] summarizes a very thorough, accurate, scientific study of patella function which he made by stating, "Experimental work shows that the patella improves the efficiency of knee extension in the more important extended positions of the knee joint by holding the patella tendon away from the axis and thereby increasing the extending movement of the quadriceps pull. Clinical investigation confirms the experimental findings."

Figure 2B shows that total removal of the patella structurally weakens the quadriceps tendon. Most of the advocates of patellectomy for simple fractures do not see and recognize the tear that is present in the tendons of the vastus medialis and vastus lateralis and in the capsule of the knee joint, simply because those tendons are hidden behind an intact and untorn layer of fascia lata; hence, one leaves the extensor mechanism of the knee much weaker in removing the patella only and not repairing the tendons of the vasti.

Therefore, total patellectomy should be reserved for those cases of disease, tumor formation or exceedingly severe compound injury which is so severe that it is absolutely impossible to achieve union with a relatively smooth articular surface by any other means. Such situations are rare. Total removal of the patella for simple fractures is seldom necessary or advisable because:

1. Complete removal of the patella structurally weakens the knee extension apparatus. (Fig. 2B.)

2. A patellectomized knee is physiologically weaker and more unstable than a normal knee [4,6,9,12,13,20].

3. A patellectomized knee is more liable to be injured again than a normal knee [15].

4. In the usual operation for patellectomy the tendons of the vasti are not sutured, although they should be.

Removal of Part of the Patella. This operation is usually performed when the lower tip or the lower one-third of the patella is fractured [22]. Fortunately, broad lateral tears are seldom found in the vasti tendons in this fracture. However, there is an open space between the remaining upper portion of the patella and the infrapatellar tendon below if these lower patellar fragments are removed. The tendon below will not stretch. It may be possible to pull the patellar tendon above, with its attached structures, down far enough to bring the infrapatellar tendon into fairly close contact with the raw, broken surface of the bone. Even if this is accomplished and if it is sutured this way, it is under considerable tension. Tissues which heal under tension will inevitably stretch and the open space partially reforms and fills with ordinary fibrous tissue which can never be as strong as the original specialized union of tendon to bone.

If strong, firm, accurate, approximation and union does not occur between the infrapatellar portion of the central quadriceps tendon and the lower end of the broken patella, it will usually be tilted upward slightly at its lower end as it rides up and down in the femoral groove. This eventually leads to chondromalacic changes underneath the patella and in the femoral groove. O'Donoghue called attention to this [19]. Compere [3] recognizes that this tilting of the patella may occur and seeks to correct it by bevelling off part of the lower anterior surface of the remaining upper patellar fragment so that tilting will be prevented as the infrapatellar tendon heals to this raw, bony surface. How much simpler it would be just to suture these torn soft tissue structures leaving the bone fragments intact. This does approximate them securely without undue tension. Partial removal of the patella for simple fractures is not desirable because:

1. Union between the infrapatellar tendon and the remaining patella is almost always weaker than the normal union.

2. If strong, firm, accurate approximation and union do not occur between the infrapatellar portion of the central quadriceps tendon and the fresh lower end of the broken patella, it will usually be tilted upward slightly at its lower end as it rides up and down in the femoral groove. This eventually leads to traumatic changes underneath the patella and in the femoral groove.

3. The operation takes much longer to perform than simple suture of the soft tissue structures around these fragments.

4. Clinical experience has shown that these knees heal more slowly and are weaker after healing than if the fragments are allowed to remain and are approximated by simply suturing the torn soft tissue snugly together.

Bone Repair. A review of the literature on patellar fractures reveals many articles which describe various means of fixing the patellar fragments. Some authors have recommended a circular suture around the patella; others fix the bone with screws, plates, loops of wire through traverse holes in the upper and lower fragment, or key-shaped grafts of bone in the anterior patellar surface. Some physicians use strips of fascia lata to hold the patella together, others use strips of infrapatellar tendon or suprapatellar tendon pulled down through drill holes in the bone. The methods that have been devised to hold the bone together are multiple, but these authors rarely recognize the tear in the tendons of the vasti and in the capsule far lateral to the patella on either side, which is hidden behind an intact and untorn layer of fascia lata.

Methods in which major attention is given only to repairing the bone are undesirable for the following reasons:

1. Not all of the torn or ruptured extensor structures are repaired. It is just as important to repair the ruptured tendons of the vasti and the capsule as it is to repair the central quadriceps tendon when the patella has been removed. Failure to repair the vasti leads to weakness of the knee in extension and the regaining of full flexion in the knee is long delayed.

2. It is exceedingly difficult by any of these methods to get the patella articular surface in absolutely smooth articular surface contact without some slight tilting being present.

3. If major attention is paid to repairing the patellar bone only and the soft tissues out to the side are not sutured, one must wait for bone union before beginning much motion in the knee, and this prolongs the patient's recovery unduly and unnecessarily.

Soft Tissue Repair. The advocates of this method of treating patellar fractures base their contentions as to its effectiveness on the following basic premises:

1. If *all* of the ruptured extensor tissues over the front and on either side of the knee are strongly, snugly sutured together, the patella fragments will be automatically brought into close accurate apposition.

2. If the knee is immobilized long enough for complete healing in the soft tissues to occur, the healed soft tissues alone will continually hold the patella fragments in close approximation without any other fixation device.

3. After complete strong healing of the fibrous tissue structures has occurred (this takes six weeks) motion may be started in the knee without the danger of the patellar fragments being separated, *because the contracting force of maturing fibrous tissue will continually and constantly hold and compress the patellar fragments together* until bony union occurs.

The first doctor who advocated the open reduction of a fractured patella was Lister [*17*]. He did note that the torn soft tissue structures should be approximated, but he did not identify all of them completely and accurately.

The earliest record I could find in which the author indicated that simple suturing of the torn soft tissue structures was all that was necessary to repair a fractured patella was written by Wilson and Cochran in 1925 [*25*]. These authors state, "As a rule it is quite sufficient to stitch together the torn edges of the aponeuroses and the fibrous covering of the patellar fragments without drilling the bone."

Lorenze Boehler [*1*] was the first to indicate that the torn vasti tendons could not be seen because of an intact layer of fascia lata. He states, "After the skin incision, the fragments are at once exposed in the middle, and laterally the uninjured fascia lata is also seen. The fascia is then incised in the direction of the skin incision and only then can one see the extent of the tear in the vastus medialis and lateralis, . . . " Groves states [*11*], "In every transverse fracture of the patella, those lateral expansions of the quadriceps tendon are torn and it is the suturing of these lateral expansions which is the most important part of the operation of repair." Trevor [*24*] emphasizes that the torn medial and lateral quadriceps expansions must be approximated.

Noyes and Mozden [*18*] state, "It must be emphasized that the patella *per se* is of secondary importance when the lateral expansions are torn and a good result is dependent upon proper suturing of the tendinous structures involved."

I saw the Lorenze Boehler operation performed several times in Vienna in 1933. On returning home, I began using it and have continued to use it simply because the results

FIG. 7. This transverse incision best exposes all torn structures.

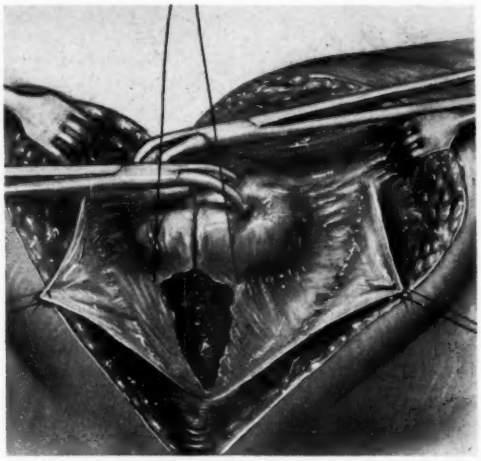

FIG. 8. Patellar fragments are pulled together with towel clamps. The suture though should be a mattress suture and a heavy, strong one. This should be carefully placed to get smooth, even approximation of patellar articular surface.

are so unusually good. A report on a follow-up study of 216 cases so treated indicates that between 80 and 90 per cent of these patients regain practically normal function of the knees and the period of time between the date of the injury and the date the patient returns to work is much shorter than is reported by most other authors [*14*].

The technic of the Lorenze Boehler operation is as follows: A long transverse skin incision is made. (Fig. 7.) The soft tissue is dissected up and down. This exposes completely the upper and lower patellar fragments and the fascia lata on either side. The fascia lata is split transversely at the level of the patellar fracture and the flaps are retracted upward and downward thus exposing the torn tendons of the vasti beneath. (Fig. 4B.) Any loose pieces of bone between the patellar fragments which may have fallen down into the joint are removed. The attached pieces are not removed.

Towel clamps are placed into each of the patellar fragments and they are pulled together. (Fig. 8.) Mattress sutures are carefully placed in the parapatellar thickenings on either side. When they are tied snugly, one will note that the articular surfaces of the patella are drawn accurately together. (Fig. 8.) Mattress sutures are used to suture the frayed, torn tendons of the vasti. (Fig. 9.) The fascia lata is sutured. The frayed strands of prepatella tendon which hang down over the raw, fractured surfaces of the patella are then retracted upward and the prepatellar portion is sutured with strong mattress sutures. When this is done, it will be noted that the patella is brought into accurate, smooth, snug contact. The sub-

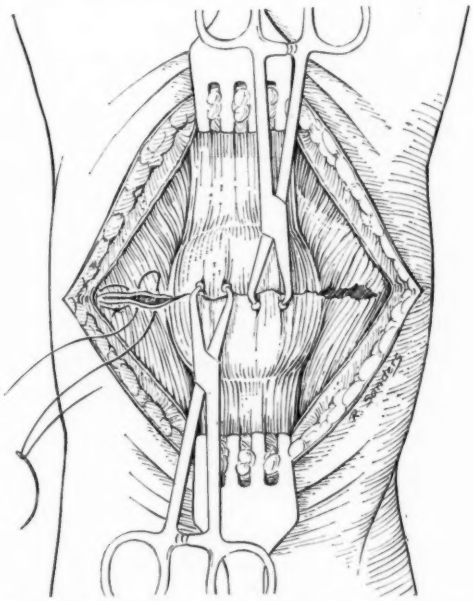

FIG. 9. Showing mattress sutures to approximate torn edges of vasti.

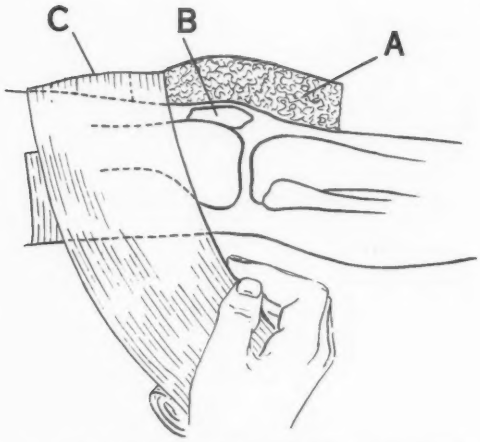

FIG. 10. (a) Large piece of foam rubber or foam plastic, (b) patella, and (c) elastic bandage compressing spongy pad against patella and patella against smooth femoral groove.

cutaneous tissue and skin are closed; the skin is usually closed with everting stitches to prevent its adherence to the tissues below.

Plaster splints are applied to each side with the leg in complete extension. A large, thick sponge plastic or sponge rubber pad is placed over the patella and is wrapped in place with an elastic bandage. (Fig. 10.) The purpose of this is to compress the articular surface of the patella against the smooth unbroken femoral groove beneath. In doing so any slight tilt or malalignment of the patellar articular surfaces is corrected. There is no better way to maintain the patella articular surfaces in perfect alignment.

The cast is often removed in three weeks because the soft tissues are healed in that length of time, *but they are not very strongly healed.* The patient then may begin moving the knee *provided he does not move it beyond the limit of pain, and provided he moves it only while he is in a standing position.* If the patient is not completely cooperative, it is better to leave the cast on for six weeks.

In three more weeks or *six weeks from the date of surgery*, the fibrous tissue structures will be completely, solidly, strongly healed and the patient may then begin active, vigorous exercises of the knee and he may begin bearing full weight on it. Within six or seven more weeks the patient usually will have normal strength in the knee, the bone will be united, the position will be good and the patient will be ready to go back to work with, for all practical purposes, a normal knee.

The operation in which a repair of the ruptured soft tissue structures of the extensor mechanism of the knee is repaired is a desirable one because:

1. It repairs *all* of the broken and torn structures.

2. It minimizes postoperative formation of scar tissue and thus allows the patient to regain motion more quickly after the knee is healed.

3. This operation effectively holds the patella in the proper position, long enough and strongly enough to permit union in the patella to occur.

4. Motion can be started earlier after this repair than with most other methods.

5. The time required to perform the operation is much shorter than by most other methods.

6. The results following such a surgical repair of the broken patella are unusually good [*14*].

Repair of Soft Tissue and Bone. No additional fixation of the fragments of the kneecap is necessary in a large percentage of cases if the soft tissue structures are accurately repaired as previously described. Once in a great while, however, there will be so much fraying of the torn parapatellar portions of the central quadriceps tendon that these sutures do not hold as snugly as they should. A circling catgut suture around the patella may be indicated in such instances.

SUMMARY

An analysis is made of all of the methods of fixing fresh fractures of the patella, and the advantages and the disadvantages of each method are discussed.

Two important anatomic features of the mechanism for extension of the knee are discussed in detail. These are so important and pertinent that anyone attempting to fix fractures of the patella should, by all means, be fully cognizant of them.

The technic of the Boehler operation and the postoperative care of the patient are described. This operation, which is a repair of the ruptured soft tissue structures only, is simple and easy to do. It can be performed quickly and it holds the patellar fragments in proper align-

ment effectively and continuously until union occurs, without the necessity of any other fixation device. The end result of this operation on soft tissue for patellar fractures is unusually good.

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SURGICAL REVIEW

Splenosis

THE AUTOTRANSPLANTATION OF SPLENIC TISSUE

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IN some instances tiny tumor-like nodules were found dispersed throughout the peritoneal cavity at autopsy or laparotomy. In most of these cases traumatic injury of the spleen could be traced in the past history. Histologic examination revealed that the nodules consisted of splenic tissue. Buchbinder and Lipkoff [6] (1939) coined the word "splenosis," a term which has been adopted in subsequent publications, to define the condition. Although the condition is rare and only thirty-six cases have been reported up to date, it merits attention on account of its pathologic implication. This communication reports an additional case and reviews the etiologic and pathologic problems of splenosis.

HISTORY

The earliest cases of splenic nodules of the peritoneum were published at the turn of the century in German literature. The first case was an incidental autopsy finding. Albrecht [1] (1896) found 400 splenic nodules in the peritoneal cavity of a young man who died of nephritis. Schilling [36] (1907) found forty-two intraperitoneal splenic nodules at another autopsy. It is noteworthy that the main organ was present but somewhat altered and smaller in both cases according to the description of the authors. In Albrecht's case the left kidney was found atrophic and imbedded in fibrous tissue. No trauma could be traced in the past history. The first case in which traumatic injury of the main organ preceded the condition was reported by Kuttner [26] (1907, operation) and Beneke [3] (1910, post mortem). Kuttner performed splenectomy for a gunshot wound of the spleen and Beneke found eighty to 100 splenic nodules in the abdominal cavity of the same patient three years later at autopsy. Faltin [12] (1911) and von Stubenrauch [42] (1912) saw the condition for the first time *in vivo* when they performed laparotomy on patients who had previously had splenectomy for traumatic injury of the organ.

After World War I, publication of sporadic cases followed with increasing frequency by Lee and Sheff [27] (1923), Kupperman [25] (1936), Buchbinder and Lipkoff [6] (1939), Krueger and Mast [24] (1942), Gill [16] (1944), Boggs [5] (1945), Waugh [45] (1946), Bunch and Spivey [7] (1946), Stobie [40] (1947), Trossero [43] (1949), Sampaio [35] (1950), Wise [47] (1953), Storsteen and Remine [41] (1953), Berry and Erdman [4] (1953), Hartman [20] (1953), Garamella and Hay [15] (1954), Cohen [10] (1954), Ferry and Cabanne [13] (1954), Pequinela [31] (1954), McCann [29] (1956), Skinner and Hurtean [38] (1957), and by Cotlar and Cerise [11] (1959). Autopsy findings were reported by Shaw and Shafi [37], Jarcho and Andersen [21] (1939), Hamrick and Bush [19] (1942), and Raper [34] (1951).

The condition was observed in experimental animals long before the first cases were detected in human pathology. Ceresole [9] (1895) states that Zambeccari described it in a dog four months after splenectomy as early as 1680. Foa [9] (1883), Tizzoni [44] (1884), Ceresole [9] (1895), and Guerrini [17] (1908) saw "nodules spleniques" in animals following incision of the capsule of the spleen.

In order to clarify the etiology of splenic

nodules, work in experimental pathology followed the publication of the first cases. Papers dealing with this subject were written by Kreuter [*23*] (1920), Marine and Manley [*28*] (1920), Putschar [*33*] (1931), Perla [*32*] (1936), Calder [*8*] (1939), and Williams [*46*] (1950).

CASE REPORT

E. S., a married female twenty-five years of age, was admitted to the hospital on November 26, 1959, complaining of intermittent abdominal pains located chiefly in the right lower quadrant. She experienced anorexia, but there was no nausea or vomiting. On further questioning, she mentioned that she had felt some abdominal discomfort for two years. She usually started to feel some heaviness in the epigastrium with vague pain which later shifted in the right lower quadrant. These complaints occurred intermittently and lasted for a few days. During the attacks she was always constipated. Seven years before her admission, she was in an automobile accident. She had been admitted as an emergency patient in another hospital where a laparotomy was performed twenty hours after the accident. A large hemoperitoneum and complete rupture of the spleen were found. The spleen was removed and she has had an uneventful recovery.

The general condition of the patient was satisfactory on admission, and the tongue was clean. No abnormalities were found on examination of the heart and lungs. The abdomen was flat. Marked tenderness with slight muscular guarding was present in the right lower quadrant. No rebound tenderness was elicited. Pelvic and rectal examination was within normal limits. Her temperature was 99.6°F. and the pulse was 92. The leukocyte count was 14,000 per cu. mm. A provisional diagnosis of acute appendicitis was made and surgery was performed.

The abdominal cavity was entered through a right gridiron incision. Small amounts of serous exudate escaped. The appendix was slightly edematous and its serosa was injected. Appendectomy was performed. On further exploration on the anterior aspect of the ascending colon, a tiny whitish nodule the size of a pea was discovered. Another nodule of brownish-red color, the size of a peanut was seen on the antimesenteric border of the ileum, 10 cm. proximal to the ileocecal junction. Both nodules were excised and the abdominal cavity was closed. Recovery was uninterrupted. When last seen six months after the operation, she was well and had no complaints.

Gross Pathology. The appendix was slightly congested but not edematous and measured 6.5 cm. in length. Complete obliteration of the lumen was seen in the distal half of the appendix while the proximal half had a minute lumen containing some brownish material.

A circumscribed kidney-shaped solid mass measuring 1.8 by 1.0 by 0.7 cm. composed the second specimen. It was smooth except for the area of attachment. This area was definitely smaller than the long cross section of the mass. The cut surface had a maroon color with grayish mottling. There was another similar but much smaller mass (0.2 cm. in diameter).

Histology. Sections of the two masses showed splenic structure even with trabeculae. It was difficult to be certain about muscle in this capsule, which was well formed. Since I found many of these structures and there was a definite history of ruptured spleen, it seemed that this was a typical case of splenosis.

The final diagnosis by the pathologist was subacute appendicitis and splenic implants (splenosis).

ETIOLOGY

The working hypotheses to explain the origin of this condition are not dissimilar to those postulated to clarify the etiology of endometriosis. Developmental anomaly, peritoneal metaplasia and transcoelomic transplantation have been claimed as etiologic factors in the same order for both conditions.

Developmental. Albrecht [*1*] (1896) and Schilling [*36*] (1907) considered splenic nodules of the peritoneum to be accessory spleens from a developmental anomaly or splitting of the splenic anlage. Accessory spleens are frequently found near the hilus of the organ, in the gastrosplenic ligament and transverse mesocolon. Splenic tissue could be detected even in the substance of the pancreas by Haberer [*18*] (1901). A common feature of this aberrant splenic tissue is that it is located in the area of distribution of the splenic artery. Even when dislocated as far as the scrotum, Sneath [*39*] (1913) believed that it derives its blood supply from a branch of the splenic artery. In histologic structure the accessory spleens are identical with the main organ; they constitute a spleen in miniature. The splenic nodules of the peritoneum do not fulfill these criteria; their distribution in the abdominal cavity as well as their histologic appearance is different.

Cellular Metaplasia. It is well known that the primitive coelomic mesothelium has varied potentialities. It was presumed by von Stubenrauch [*42*] (1912) that the peritoneum preserves some of these abilities. Thus, loss of the spleen would stimulate the dormant spleen-forming

capacity of the peritoneum, which would result in the development of splenic nodules. A variant of this conception is the view put forward by Tizzoni [44] (1882), who considered the possibility of peritoneal metaplasia as a manifestation of atavistic reversion. In the lower vertebrates, Cyclostomae, some cavernous lymphatic spaces along the mid-gut represent the first vestige of the spleen in the phylogenetic development. According to Tizzoni loss of the main organ would stimulate this atavism. However, real atavism, would result in the development of cavernous lymph spaces in the intestinal wall rather than splenic tissue. This point seemingly escaped the author's attention. No experimental evidence could be produced in support of the conception of cellular metaplasia.

Transcoelomic Transplantation. There is much experimental and clinical evidence that the splenic nodules of the peritoneum are seedlings, that is, the result of successful grafting following transcoelomic dispersion of particles of the splenic pulp. The autotransplantability of the splenic tissue was demonstrated by several authors: von Stubenrauch, Kreuter, Marine and Manley, and Perla. Conclusive evidence for successful grafting subsequent to injury of the main organ was brought by Kreuter. He demonstrated in a series of experiments that complete removal of the organ was not followed by the development of implants when the capsule was not damaged and no pulp could escape. Subtotal splenectomy resulted in the development of a few nodules in the vicinity of the stump, whereas nodules were found disseminated throughout the abdominal cavity ensuing smearing of the pulp on the peritoneum.

Putschar (1931), by his follow-up studies of splenic peritoneal grafts, later refuted von Stubenrauch's assumption that the splenic transplants would regress and be replaced by splenoid tissue resulted from the metaplasia of the peritoneum.

Accumulating clinical experience gave further support to the transcoelomic transplantation. In the great majority of cases traumatic rupture of the spleen antedated the development of splenosis. Furthermore, the distribution of the nodules in the peritoneal cavity is not dissimilar to that of malignant secondaries, and one has the impression that gravity is a determining factor in both conditions. Finally, the histologic appearance of the nodules is similar to that of the autotransplants in experiments with animals.

PATHOLOGY

Distribution. Autopsy findings demonstrated that the lesion can involve the whole peritoneal cavity. Table 1 shows the topographic distribution of eighty intraperitoneal splenic nodules. It is evident that the diaphragm, the great omentum and the ileum are favored as sites of implantation. The parietal peritoneum seems to be immune with the exception of two areas, the scar of the laparotomy and an incidental hernial sac. What factors determine the spread and distribution of the escaped pulp fragments is a question open to speculation. Probably the concomitant hemoperitoneum plays some role as well as the recumbency after the injury of the spleen. Gravity may be considered as another factor.

Macroscopic Appearance. The splenic nodules are usually sessile, subserous growths of variable sizes ranging from that of a pinhead to masses 3 cm. in diameter. The small nodules are grayish-white; the larger ones have the color and consistency of the spleen. (Fig. 1.) They receive their blood supply through vessels entering on the circumference of their attachment, but no hilus is discernible.

Histology. There is a marked difference between the histologic appearance of a splenic nodule of the peritoneum and that of the main organ or of an accessory spleen. This difference reflects itself especially in the capsule and the white pulp.

The capsule of the nodule is usually a layer

TABLE 1
INTRAPERITONEAL DISTRIBUTION OF SPLENIC NODULES*

Location	No. of Patients
Parietal peritoneum, incisional scar	9
Diaphragm	17
Cul-de-sac of Douglas	7
Great omentum	15
Mesentery	4
Gastrohepatic omentum	2
Stomach	6
Small intestine	16
Large intestine	2
Gallbladder	1
Left ureter	1

* Shaw and Shafi's case.

FIG. 1. Splenic nodule removed from the ileum, in longitudinal section. Concave border marks the surface of its attachment. The fibrotic tissue in the central area is probably the remnant of early central necrosis.

of fibrous tissue, but no smooth muscle or elastic elements are discernible. Its thickness is variable; here and there it is penetrated by lymphocytes which infiltrate the pericapsular area as well. Large lymphatics can be seen among the extracapsular lymphocytic agglomerates. The trabeculae show the same structure as the capsule. At their origin, the penetrating blood vessels sometimes mimic a hilus formation. (Fig. 2.) In conclusion, the capsule and trabeculae of the nodule are less differentiated structures than those of the spleen.

A lesser degree of differentiation is manifest in the white pulp too. The malpighian bodies are scarce and less well demarcated. In some of them, central penicillar-artery can be seen. (Fig. 3.) In many places they are rather simple agglomerates of lymphoids than lymph follicles. The nodules showed morphologic signs of activity. Iron deposits were found in the cells of the pulp and even miliary tubercles containing Mycobacteria were described in a patient suffering from tuberculous infection [37].

Histogenesis of the Splenic Transplant. It is appropriate to include this item in pathology as data derived from experimental transplantation can throw some light on the different histologic appearance of the splenic nodule. The fate of a splenic transplant and the changes which ensue implantation transplantation are similar to that of an autogenous bone graft. It is to facilitate description that the changes occurring during implantation arbitrarily are divided into the following four stages:

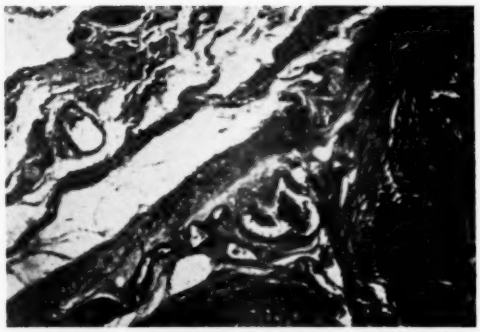

FIG. 2. Section showing the site of penetration of blood vessels and a hilus-like area at the origin of one of the trabeculae.

1. Mobilization of the cellular constituents. Immediately after implantation the mobile cells (lymphocytes, plasmocytes, mononuclears) leave the pulp spaces and penetrate into the surrounding tissue. The reticulum cells detach themselves and become macrophages. The endothelial cells lining the sinuses follow suit. Fourteen hours after the implantation all the constituents of the reticuloendothelial system in the transplant are mobilized.

2. Necrobiosis of the central portion. This change occurs concomitantly with the previous one. When it is deprived of its blood supply, the central area dies as in an autogenous bone graft. Morphologic signs of necrosis appear later, but macrophages invade the central part as soon as eighteen hours after implantation [33].

3. Vascularization of the graft. Capillaries from the neighboring tissues make their appearance in the graft the third and fourth day

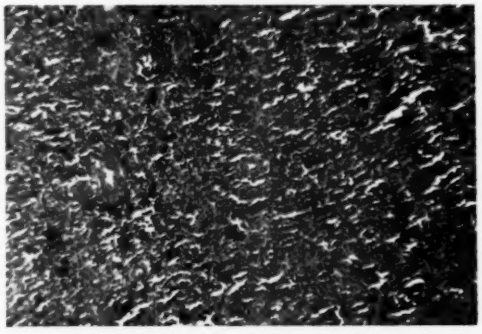

FIG. 3. Microphotograph of the pulp showing in the center a penicillar artery surrounded by lymphoid tissue.

TABLE II
AGE AND SEX INCIDENCE OF SPLENOSIS

Age Group (yrs.)	Men	Women	Total
0–10	1	1	2
11–20	12	4	16
21–30	9	3	12
31–40		2	2
41–50	1	2	3
51–60	2		2

after implantation according to Calder [*8*]. Putschar more cautiously put the first appearance of the newly formed capillaries on the tenth day.

4. Organization of the graft. When completely vascularized, around the twenty-fourth day, aggregates of lymphocytes pervade the whole graft so that it has the appearance of a lymphoid structure rather than splenic tissue. This aspect changes slowly as the lymphocytes gradually gather around the blood vessels.

It is probable that only the red pulp of the splenic nodule is of splenic origin. Its capsule is derived from the surrounding tissue. The successful grafting, as the experimental transplantation shows, is due to the unique ability of the reticulum cells of the graft, not only to survive in the critical period until the graft takes, but also to transform into macrophages and clean the field [*8,32*]. The host tissue reaction is reduced accordingly to the minimum, that is, to the formation of the capsule.

CLINICAL FEATURES

In the great majority of the published cases, traumatic injury of the spleen followed by splenectomy could be elicited in the past history. The interval between the accident and the detection of splenosis ranged from six months to thirty years, the majority being diagnosed in the first five years following the trauma or splenectomy. The real incidence of the condition can not be ascertained since a certain proportion of cases probably remain undetected. The age and sex incidence correspond with that of traumatic injury of the spleen; most of the cases fall in the second and third decades of life, more than twice as many males being affected as females. (Table II.)

Symptoms and Signs. The majority of cases was detected incidentally at surgical reexploration of the abdominal cavity for another condition, such as intestinal obstruction, appendicitis, hernioplasty. Although it seems that the disease has no symptomatology of its own, retrospective questioning revealed that most of the cases suffered from intermittent abdominal discomfort. It is uncertain whether this is due to adhesions, to the presence of splenic nodules or to the loss of the spleen as some authors suppose [*2*]. These authors followed up 209 patients previously subjected to splenectomy for traumatic injury. They found the following: abdominal pains, ninety-six cases (48 per cent); night sweats and clammy hands, seventy-seven cases (35 per cent); blackouts and fainting attacks, seventy-four cases (34 per cent); persistent tiredness seventy-three cases (34 per cent); and intolerance to alcohol in adults previously unaffected, fifty per cent.

They conclude that loss of a normal spleen would cause some disorder in the autonomic nervous function, manifesting itself as vasomotor instability. Intolerance to alcohol is explained by the loss of detoxicating function of the spleen. None of these symptoms could be detected in the present case.

Diagnosis. Preoperative diagnosis rests on presumption in a case presenting vague abdominal discomfort and a history of splenectomy.

The operative diagnosis is not easy even if the disease is considered. The splenic nodule has to be differentiated from other nodular lesions of the peritoneum, such as endometrioma, hemangioma, encapsulated foreign bodies, and malignant metastases. Endometriomas inducing a pronounced fibrosis are usually not sessile but more deeply imbedded in the intestinal wall. Hemangiomas have the same appearance as the splenic nodules, but they are compressible and refill after pressure is released. Encapsulated foreign bodies (food particles following peptic ulcer perforation) are whitish-gray in color. Fibrin deposits in hernial sac are usually present and have the same appearance as the former. Malignant metastases of the peritoneum usually form yellowish-white, umbilicated nodules or plaque-like masses.

TREATMENT

McCann [*29*] suggested the flushing of the peritoneal cavity with saline as a preventive measure after splenectomy is performed in

TABLE III
RECORDS OF SPLENOSIS

Author	Year	Age (yrs.)	Diagnosis*	Site of Nodules	Interval Since Splenectomy (yrs.)
Albrecht	1896	25	Autopsy	Whole peritoneal cavity	
Schilling	1907	47	Autopsy	Whole peritoneal cavity	
Kuttner	1910		Autopsy	Whole peritoneal cavity	3
Faltin	1911	9	Appendectomy	Appendix, cecum, ileum	6
von Stubenrauch	1912		Intestinal obstruction	Great omentum transverse mesocolon	11†
Oltmann	1919		Autopsy	Whole peritoneal cavity	
Jolly	1919	15	Exploratory laparotomy	Great omentum	
Lee and Sheff	1923	29	Intestinal obstruction repair	Ileum, mesentery	15
Kupperman	1936	15	Incisional hernia repair	Whole abdominal cavity	6†
Shaw and Shafi	1937	20	Autopsy	See Table 1	
Jarcho and Andersen	1939	8	Autopsy	Whole peritoneal cavity	2
Jarcho and Andersen	1939	20	Autopsy	Whole peritoneal cavity	8
Buchbinder and Lipkoff	1939	28	Exploratory laparotomy	Whole peritoneal cavity	19
Hamrick and Bush	1942	12	Autopsy	Whole peritoneal cavity	3
Krueger and Mast	1942	16	Intestinal obstruction repair	Great omentum	5
Gill	1944	54	Bullet-wound scar excision	Thoracic wall	2
Boggs	1945	14	Appendectomy	Appendix, ileum	3
Waugh	1946	37	Hysterectomy	Ileum, cecum	5
Bunch and Spivey	1946	12	Appendectomy	Great omentum, pelvis, mesentery	3
Stobie	1947	29	Caesarean section	Uterus, omentum, pelvis	4
Trossero	1949	41	Inguinal hernioplasty	Parietal peritoneum	4
Trossero	1949	56	Laparotomy	Great omentum	
Sampaio	1950	19	Appendectomy	Ileum, mesentery, cecum	10
Raper	1951	30	Autopsy	Whole abdominal cavity	
Wise	1953	24	Intestinal obstruction repair	Great omentum	10†
Storsteen and Remine	1953	22	Intestinal obstruction repair	Whole abdominal cavity	5
Berry and Erdman	1953	14	Intestinal obstruction	Mesentery, omentum, ileum	2
Hartman	1953	31	Exploratory laparotomy	Small intestine, pelvis	1
Garamella and Hay	1954	22	Appendectomy	Ileum, mesentery	
Cohen	1954	30	Scar excision	Splenectomy scar	22
Ferry and Cabanne	1954	23	Incisional hernia repair	Ileuum	10
Pequinela	1954	46	Intestinal obstruction repair	Ileum, cecum	12
McCann	1956	45	Laparotomy	Whole abdominal cavity	30
Skinner and Hurtean	1957	29	Exploratory thoracotomy	Pleural cavity	10
Cotlar and Cerise	1958	17	Intestinal obstruction repair	Small bowel, mesentery, great omentum	5
Cotlar and Cerise	1958	20	Intestinal obstruction	Jejunum	2
Szabo	1959	25	Appendectomy	Ileum, cecum	7

* The time that diagnosis was made is indicated.
† Months are indicated rather than years.

order to remove escaped fragments of the pulp. As curative treatment, although the disease is benign, it is advisable to remove the larger nodules in order to eliminate eventual mechanical interference resulting from their presence.

SUMMARY

The literature concerning this problem is reviewed and an additional case is reported. The etiology, pathology and clinical feature of splenosis is discussed.

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A Practical Technic for the Routine Use of Operative Cholangiography

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THE preferred management of a stone within the extrahepatic biliary system is its recognition and removal. The role of operative cholangiography in detecting overlooked stones in the common duct remains controversial. The controversy revolves around the accuracy of its use versus the alleged disadvantages of the procedure.

An earlier report of 444 patients undergoing operative cholangiography during biliary tract surgery [1] cited a diagnostic accuracy of 88 per cent. Subsequent experience with 152 additional patients reveals the diagnostic accuracy to be comparable.

Many of the disadvantages attributed to operative cholangiography stem from the limitations of the procedure either because of errors in technic or errors in interpretation of the cholangiograms. Similarly, many of the interpretative errors result from the technically poor films available for inspection, whether this fault resides with the surgeon or the radiologist. Likewise, faulty technic is usually responsible for the objections that operative cholangiography is "tedious," "cumbersome," or "time consuming." The merit of recognizing overlooked stones with the abdomen of the anesthetized patient opened and the surgeon in a position to remove the stones requires no further comment. Many surgeons who question the accuracy of operating room cholangiography routinely use delayed cholangiography in the postoperative period prior to removing a T tube placed into the common duct during operative exploration. The inertia of a surgeon to use a procedure in the operating room when he customarily employs this same procedure in the roentgenology section must result from his dissatisfaction with the technical performance of the examination in surgery.

From a review of over 2,600 cholangiograms on 596 patients undergoing operative cholangiography during biliary tract surgery certain technical pitfalls of the procedure have been recognized. It is the purpose of this report to cite a practical technic for the routine performance of operative cholangiography.

The preanesthetic medication includes a barbiturate and scopalamine. Morphine is avoided preoperatively because it induces spasm of the ampullary muscle. The patient is positioned on the operating table with the right upper quadrant centered over a cassette holder preferably, but not necessarily, equipped with a Bucky diaphragm. The opening in the cassette holder for replacing the exposed films should be on the patient's left side. The cone of a portable x-ray unit is centered over the area of the gallbladder at a distance of 36 inches from the skin. A preliminary exposure with radiographic factors of 30 milliamperes and 90 kilovolts for one second is taken prior to preparing and draping the patient. The film is developed immediately to insure proper positioning and to check the radiologic factors.

When the patient is washed and prepared, towels are sutured to the skin preparatory to placement of the laparotomy sheet. Similarly, wound drapes are sutured to Scarpa's fascia after the incision has been made. Towel clips are avoided in the draping because of their radiopacity.

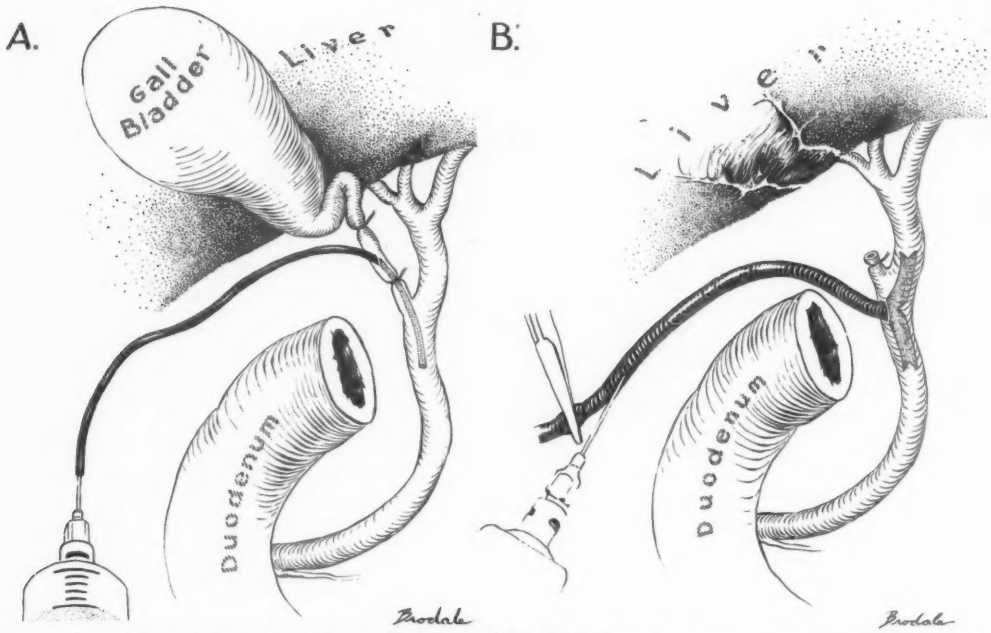

FIG. 1. A, polythene catheter is in place for instillation of the media into the common duct. B, instillation of the media through the T tube into the duct system after cholecystectomy.

Following manual palpation of the contents of the peritoneal cavity, the right upper quadrant is exposed and packed in the usual manner for cholecystectomy. The cystic duct is exposed, isolated and ligated about 2 cm. from its entrance into the common duct in order to confine the contents of the gallbladder as well as to maintain traction while exposing the distal cystic duct. A second suture is placed intramurally into the cystic duct approximately 8 mm. closer to the common duct. A small transverse incision is placed in the cystic duct between the two ligatures and a No. 17 polythene catheter (at least 24 inches long) is threaded through the cystic duct into the common duct for a distance of 1 cm. If difficulty is encountered passing the catheter through the cystic duct, preliminary dilatation of the valves of Heister with a rectal probe will usually insure successful passage of the polythene tubing. The second ligature is then tied about the distal cystic duct to maintain the catheter in place as well as to prevent extravasation of the contrast agent. The polythene tubing is then brought out through the incision with the end placed over the patient's side to allow bile to flow through the tubing into the syringe, thus eliminating air from the system. All retractors, sponges and radiopaque objects are removed from the operative area. A towel is draped over the incision and a blood stain placed on the towel as a guide for the radiologic technician to center his cone. The syringe containing 20 cc. of 50 per cent solution of Hypaque is attached to the polythene catheter and supported on the drapes over the right thigh. (Fig. 1A.) The ductal system is not irrigated with saline solution prior to instillation of the media as intensive flushing often produces bubbling with concomitant interpretive errors. Air is satisfactorily eliminated from the tubing by the aspiration of bile into the syringe.

Following the introduction of 5 cc. of the contrast media over a one-minute period, the surgeon signals to the anesthesiologist who, on rendering the patient apneic, directs the technician to expose the film with the command "shoot." As the technician replaces the cassette the surgeon has already begun the second instillation of 5 cc. of the contrast agent. Similarly, the anesthesiologist will direct

the technician to expose the film during a period of apnea. A third injection, this time with 10 cc. of the contrast agent, again commences while the technician is replacing the film. Instillation of the media is performed over a two-minute period. While the films are being developed the gallbladder is removed to prevent undue prolongation of the operating time. The fractional method of instillation allowing three cholangiograms for study has certain advantages. The initial film with 5 cc. of a concentrated media allows sufficient contrast of the duct structure but is less apt to obscure stones than the completely filled biliary ducts with a single larger amount of agent. Also, the merit of two additional films for evaluating a suspicious intraductal filling defect, air bubbles, or indentation which may be present on one of the cholangiograms is apparent. Information is gained about the sphincter of Oddi from the manner of flow into the duodenum of small amounts of contrast media under low pressure. Likewise, motion during exposure of one of the films will not negate the value of the procedure.

Postexploratory cholangiography performed through the T tube after exploration of the common duct serves as additional insurance against retained common duct stones. (Fig 1B.) The technical performance of postexploratory operative cholangiography resembles that of the pre-exploratory technic with minor variations. It has been noted that the area within the common duct occupied by the ascending and descending limbs of the T tube is not satisfactorily visualized by cholangiography. A common site of error of interpretation of the cholangiogram is a radiolucency at the end of the descending limb produced by end-on viewing of the T tube or by pressure of the T tube against the wall of the common duct. These errors may be minimized by inserting a T tube into the duct with the ascending and descending limbs each measuring approximately 1 cm. This places any area of suspicion easily within reach of the palpating fingers. Extravasation of the media at the site of closure of the common duct about the T tube is negligible if the instillation of the contrast agent is performed slowly to maintain a low intraductal pressure. Saline solution is flushed through the T tube and the ductal system is irrigated gently when T tube cholangiography is performed as the preceding operative exploration usually introduces air into the ducts. The initial exposure is made with 8 cc. of the contrast agent to allow for the media which will occupy the T tube. Additional increments of 5 cc. and 10 cc. for the second and third exposures are made in similar manner as for the pre-exploratory technic.

Operative cholangiography has a useful place in the surgery for acute cholecystitis. However, the marked edema about the gallbladder and adjacent structures requires a variation in the routine approach to pre-exploratory cholangiography in the patient with acute cholecystitis. The gallbladder is usually removed in a retrograde manner to expose the cystic duct. Between right angle clamps the cystic duct is transected below the point of obstruction and the edematous organ removed to facilitate vision of the cystic duct. A polythene catheter is then inserted through the cystic duct remnant into the common duct and cholangiography executed in the usual manner. Following the final x-ray exposure, the catheter is removed and the redundant remnant of cystic duct excised.

It is believed that acute cholecystitis represents a complicating incident in the course of chronic cholecystitis with cholelithiasis rather than a separate disease entity. Accordingly, a recovery rate of common duct stones in patients with acute cholecystitis has been found to approximate that when elective cholecystectomy is performed for chronic gallbladder disease [4].

Upon review of the cholangiograms certain pitfalls may be apparent. If the intrahepatic ductal structures are not adequately filled, the patient is placed in the Trendelenberg position and an additional 5 cc. of media injected. The left hepatic duct should be filled for at least 2 inches and both the dorsocaudal and ventrocranial branches of the right hepatic duct visualized for a satisfactory examination. Failure of the contrast media to pass into the duodenum on the third cholangiogram is usually indicative of obstruction at the ampulla. This may be due to stone, fibrosis, or spasm of the sphincter of Oddi. Occasionally, a dilated ductal system may occupy all the media. When none of the media has entered the duodenum, the anesthesiologist will tilt the table placing the patient in a reverse Trendelenberg position. An x-ray exposure is made. Then $\frac{1}{100}$ gr. of nitroglycerine is placed sublingually, an addi-

tional 5 cc. of contrast agent instilled into the ducts and a second exposure made. In a patient with spasm of the sphincter, contrast media usually enters the duodenum on the film exposed after the nitroglycerine has been given.

The pancreatic duct is visualized cholangiographically in approximately 40 per cent of the patients when the media is instilled under low pressure. A forceful injection of the contrast agent, however, will cause reflux into the pancreatic duct in nearly double this number. A transient elevation of the serum amylase level six to eighteen hours after cholangiography is noted four times as frequently when reflux occurs into the pancreatic duct. While this would appear to be due to a mild transient pancreatic necrosis, it has not influenced the immediate postoperative recovery of the patients. Acute pancreatitis occurred in less than 0.5 per cent of the patients in this series in whom operative cholangiography was used with biliary tract surgery. This compares favorably with the incidence of pancreatitis in biliary tract surgery when cholangiography is not used.

While the complications of operative cholangiography will be the subject of a subsequent report, it is noted that extravasation of the contrast media, occurring to some degree in 11 per cent of the patients, has been of negligible consequence.

SUMMARY

A simple, practical technic evolving from an experience with 596 patients undergoing operative cholangiography during biliary tract surgery is presented. It is apparent that consistent success with the routine use of this procedure requires a cooperative effort between the surgeon, anesthesiologist, radiologist and radiologic technician.

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Control of Gastric Function After Subtotal Gastrectomy

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OPERATIONS performed for the cure of peptic ulcer have as their main purpose the elimination of acid pepsin. This is accomplished by partial excision of the stomach and by the removal of hormonal factors and vagal stimulation. This approach to the problem is both rational and fundamental, but in concentrating upon it there has been a tendency to underemphasize other important considerations.

In the upright position the normal stomach has its outlet at a higher level than the dependent portion of the sac, and it also has been provided with a valve to assure proper gastric function. This results in a gastric emptying time of from three to four and a half hours.

It would seem reasonable after subtotal gastrectomy to reconstruct a pouch that performs its function in the same normal manner that nature had originally intended. In addition to the elimination of the acid pepsin factor, careful consideration should be given to the two available buffers: first, the alkaline secretions from the liver, pancreas, and duodenum; secondly, the ingested food.

Much attention has been given to the size of the residual gastric pouch following subtotal gastrectomy but little to its shape and function. Although the size is important, its importance tends to be minimized if it does not retain food for any appreciable period of time. The reconstruction should also be performed in a manner that will allow for the maximum benefit of alkaline secretions. If food is not retained for a reasonable period and the secretions are shunted rapidly past the stoma, an ideal situation exists for recurrence of ulcer and other postgastrectomy complications.

I suggest that too much emphasis has been placed upon methods in assessing either good or unsatisfactory results. Comparisons between the Billroth I and Billroth II operations are constantly being made rather than efforts to discover the reason for success or failure in either instance. Analyses of these results are usually made as a group and expressed by a percentage. It is more logical to concentrate upon the reasons for failure than to assume that the method itself is at fault.

With such thoughts in mind, I have attempted to reconstruct a gastric pouch that functions physiologically and empties in a normal manner. The results have been sufficiently impressive to warrant a report of this experience. Studies of gastric function have been made in a representative number of cases in an attempt to explain the variability of results.

TECHNIC

The modification of the Billroth II operation that has been used in a consecutive series of 135 personally performed operations, with a follow-up of from one to seven years, has as its major

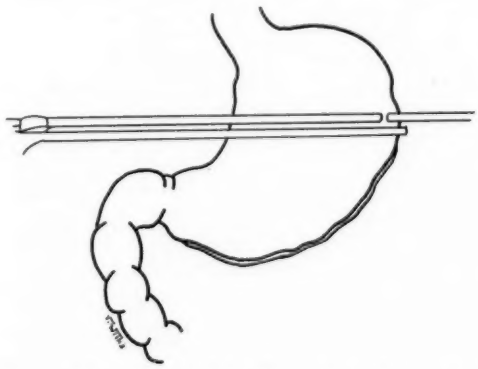


FIG. 1. Method of applying Payr clamps in carrying out resection.

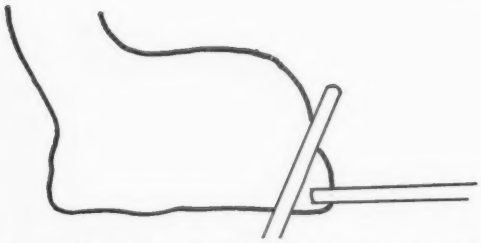


FIG. 2. The cut lower border has been closed with a running suture over the clamp beginning at side of the lesser curvature and, after removal of the clamp, the same suture is run back to the starting point and tied. This suture line is inverted with interrupted silk. A small Payr clamp is applied vertically regulating the size of the stoma.

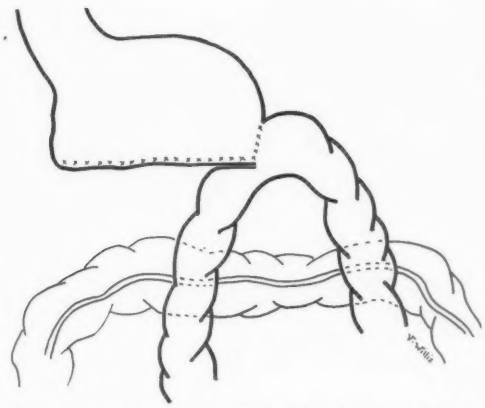


FIG. 3. Completed anastomosis. Note horizontal lower border and direction of flow into the efferent loop.

aim a normally functioning gastric pouch after resection of approximately two-thirds of the stomach. A short antecolic anastomosis is utilized with careful attention to the size of the outlet and to its location. The lower border of the stomach is closed horizontally, avoiding a steep slope from the lesser curvature which tends to cascade food into the opening. The stoma is placed on the greater curvature and is slightly less than the diameter of the jejunum. (Figs. 1, 2 and 3.) The average distance of the afferent loop from the ligament of Treitz is two and a half to three and a half inches. The ease with which a short loop can be brought up depends upon the length of the mesentery and not the distance from this ligament. Tension is eliminated by bringing up the jejunal loop to the left of the midline where there is no low transverse colon and a minimal amount of great omentum. This leaves the efferent loop free on the left side of the abdominal cavity with the great omentum lying to the right.

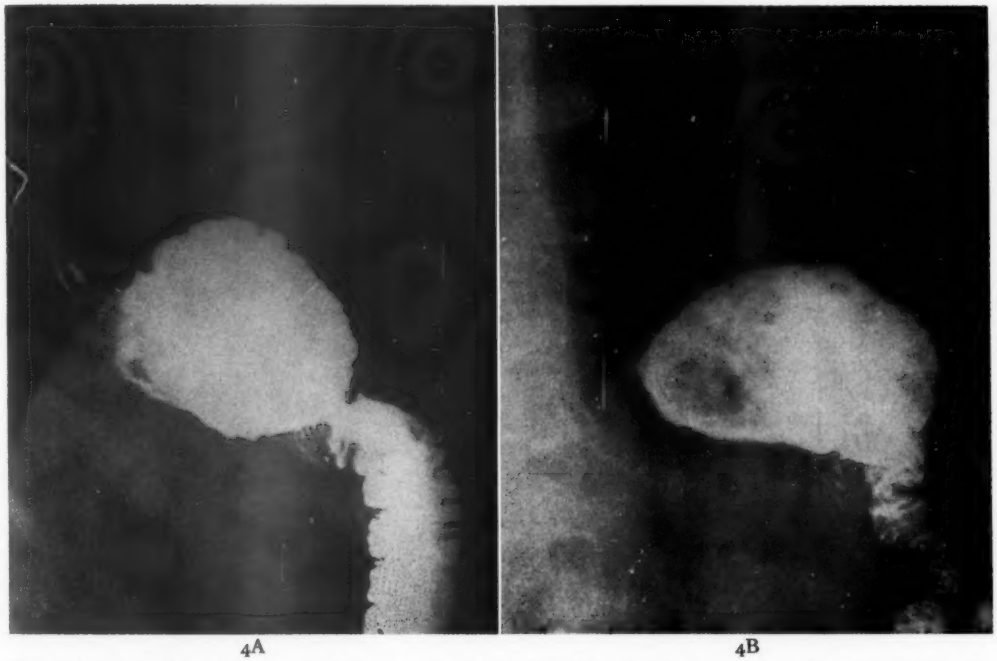
This technic has the following desirable features: (1) the gravity factor is diminished and emptying of gastric contents is slowed down to a normal rate; (2) the direction of flow from the stomach is horizontal and into the efferent loop eliminating afferent loop flooding which is a well known cause of postgastrectomy disturbance; and (3) alkaline secretions are brought to a higher level to allow constant regurgitation into the pouch which seems more desirable than to have it pass along a dependent gutter.

My general objection to a dependent anastomosis, although it may work perfectly well in a fair percentage of cases, is the difficulty in controlling the passage of food from the stomach into the jejunum. After this operation food is retained within the stomach until it passes into the efferent jejunal loop. After the routine Polya and Hofmeister procedures, on the other hand, food passes from the stomach into a dependent jejunal loop before reaching the efferent opening. If an attempt is made to slow gastric emptying by narrowing the outlet, it is obvious that back flow into the afferent loop will occur automatically.

GASTRIC FUNCTION STUDIES

In order to determine how successful the major aim of constructing a normal functioning gastric pouch is, gastric function studies were made postoperatively on seventy-one of the 135 cases. Studies were also made on a smaller series of normal individuals and on postoperative patients who had had subtotal gastrectomy performed by other routine methods.

Through the cooperation of the dietary department of the Rhode Island Hospital, a sandwich meal which represented a cross section of the average luncheon served at the hospital was made. It contained 30 gm. of carbohydrate, 28 gm. of fat, and 12 gm. of protein, a total of 420 calories. This meal was given with a small swallow of barium and serial roentgenograms were taken at half hour intervals until the gastric pouch was empty. A characteristic pattern was noted in the large majority of cases performed by the present technic. It consisted of a gradual and intermit-



4A 4B

FIG. 4. A and B, characteristic x-ray films demonstrating filling of the gastric pouch. Note the direct entry of the mixture into the efferent loop and absence of filling of afferent loop.

tent emptying of the pouch by a jet-like action. The average emptying time was from two to four hours and in some cases a small amount of residue remained for even longer periods. The direction of flow was into the efferent loop with only slight or occasional filling of the short afferent limb. In no instance was there flooding or dilatation.

Figures 4A and B are typical illustrations of the early filling of the pouch showing absence of filling in the afferent loop and initial emptying of the gastric remnant. It is most gratifying to observe the gradual emptying of the pouch and the slow filling of the jejunum.

Figures 5, 6A and B (Case 1) illustrate the distribution of the barium mixture at various intervals. It will be noted that there is no visualization of the afferent loop. In Figure 5 the mixture is seen to be slowly filling the upper jejunum at the end of a half hour. At the end of one and a half hours (Fig. 6A) the food mixture is well distributed throughout the small bowel and the stomach continues to empty slowly. In Figure 6B the mixture has reached the colon with a small amount of residue still in the gastric pouch at the end of two and a half hours. It will be remembered that food remains in the stom-

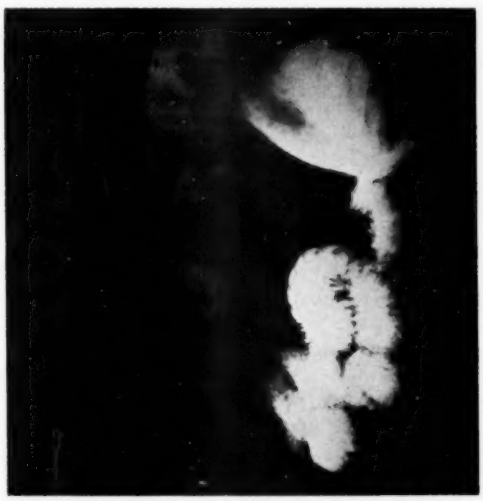
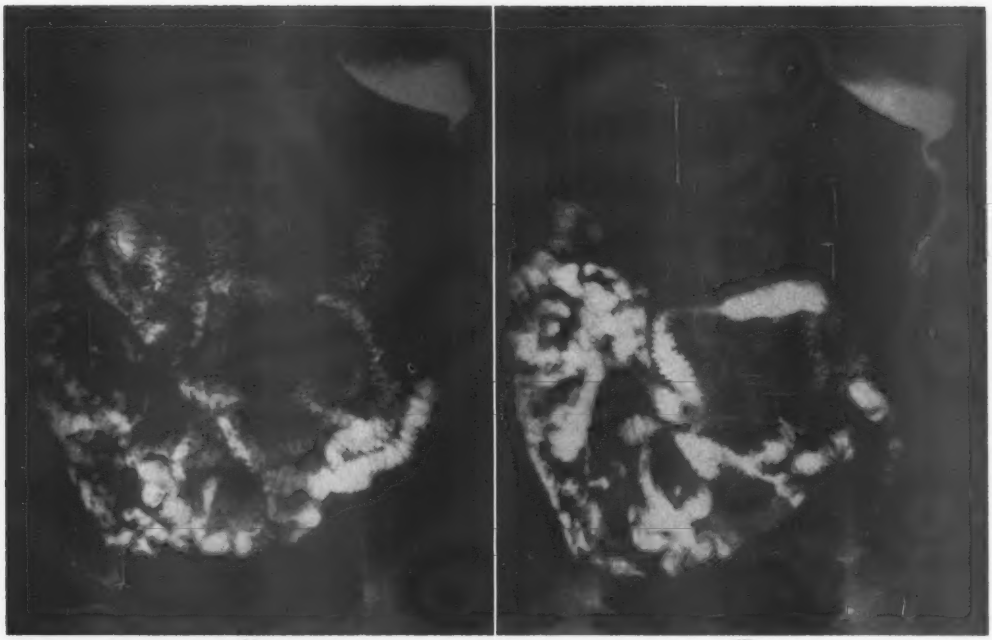


FIG. 5. Case 1. X-ray film taken a half hour after the ingestion of barium mixture. The stomach has begun to empty slowly and the proximal jejunum has filled.



6A 6B

FIG. 6. Case I. A, illustrates the distribution of the barium mixture after one and a half hours and B, after two and a half hours. Note that the gastric pouch is still partially filled.

ach from three to four and a half hours in the normal individual. Case I, which represents the typical pattern observed in patients operated upon by the present technic, illustrates normal gastric function following subtotal gastrectomy.

Figures 7A and B (Case II) show the characteristic food pattern after a half hour and two and a half hours with the stomach still containing a moderate amount of the food mixture.

Figure 8A (Case III) illustrates a third case two and a half hours after the barium mixture had been given. It will be noted that the meal has reached the colon and that the pouch still contains a moderate amount of the mixture.

In contrast to the above cases that demonstrate normal gastric function, Figure 8B illustrates the construction of a pouch in which the food mixture is poorly retained. This patient was operated upon in another city, and a dependent Hofmeister anastomosis had been performed. Distention of the afferent loop and almost complete flooding of the small bowel at the end of a half hour was observed. When first seen, this patient had experienced reduction in weight from 120 to 80 pounds and had the severest type of dumping symptoms.

In seventy-one cases in which the barium studies were made, the large majority showed normal gastric function as illustrated in Cases I, II and III. In these, the food remained within the gastric pouch from two to four hours and showed gradual filling of the small bowel as the stomach emptied. However, a perfect functional result was not obtained in some patients due to minor errors in technic. Fortunately, these deviations from the ideal were slight and rarely resulted in symptoms that were disturbing. The important fact noted, however, was that normal function was observed if the operation was properly performed according to the technic described herein. I believe that the attention given to the technical details of fashioning the pouch, along with accurate placement of the stoma which should be less than the diameter of the jejunum, is usually responsible for success or failure.

Of the seventy-one cases in which gastric studies were made, the correlation between normal function and excellent results was striking.

7A 7B

FIG. 7. Case 11. Another example of normal emptying of the gastric pouch. A, at the end of a half hour and B, at the end of two and a half hours.

ANALYSIS OF CASES

The 135 cases presented represent a typical cross section of the problem encountered in the surgical treatment of peptic ulcer. This is a consecutive personal series and includes all age groups and all cases of massive hemorrhage.

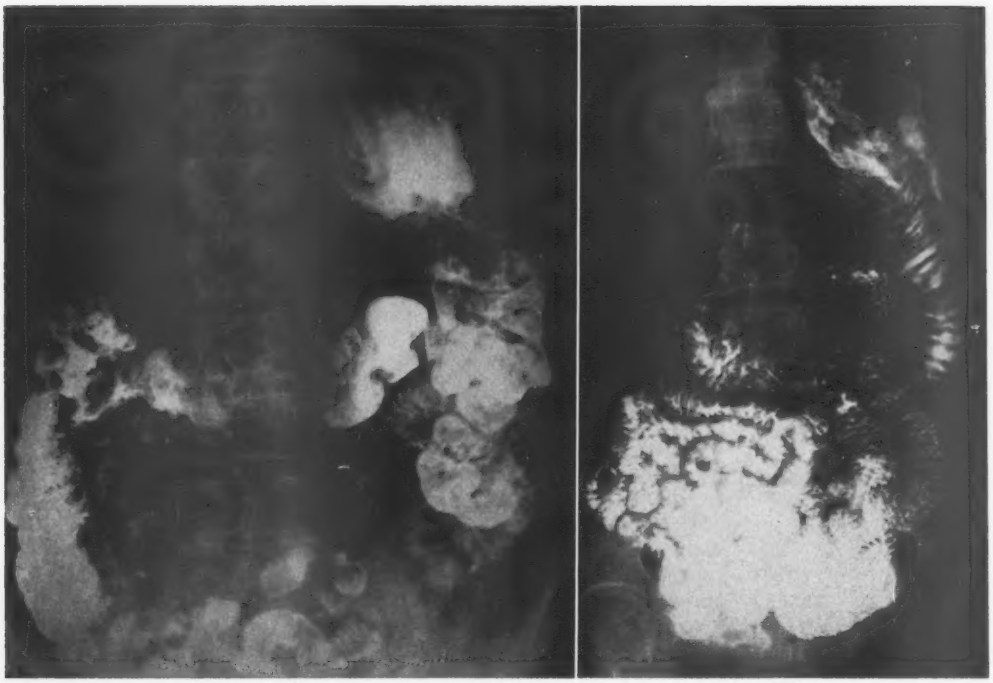
There were ninety patients fifty years of age or over and only five below the age of forty. The oldest was eighty-three and the youngest thirty-two years of age. (Table 1.)

There were eighty-eight duodenal ulcers, thirty-seven gastric ulcers, three marginal ulcers, and one that showed both a duodenal and a gastric ulcer. The six patients in whom no ulcer was found were operated upon for massive, uncontrollable gastric hemorrhage. The sex distribution according to the ulcer found is illustrated in Table 11.

There were fifty-one cases in which hemorrhage occurred. Of these, twelve were severe, seventeen were moderate, and twenty-two were mild. "Severe" was interpreted as those patients who entered the hospital bleeding with a hemoglobin level below 5 gm. or in shock. X-ray studies were usually made in cases of bleeding. (Table 111.)

TABLE 1
AGE RANGE OF PATIENTS

Age (yr.)	No. of Patients
30–39	5
40–49	40
50–59	56
60–69	24
70–79	9
Over 80	1
Total	135



8A 8B

FIG. 8. Case III. A, illustrating a third case two and a half hours after the mixture had been given. B, example of rapid emptying of an improperly constructed gastric pouch with flooding of the small bowel at the end of a half hour.

Although a longer period of follow up is always desirable in the study of recurrence of ulcer, a shorter period at least demonstrates (1) whether or not the patient can maintain a normal weight, and (2) if the operation is to be followed with symptoms of dumping. (Table IV.)

Twenty-eight associated operations were performed. This figure does not include appendectomies. Esophageal hiatus hernia was repaired fourteen times. I believe that patients who are having ulcer-like symptoms and in whom both peptic ulcer and hiatus hernia are present, should have both corrected since it is difficult to be certain which condition is responsible. Frequently both lesions are symptomatic. Since repair of esophageal hiatus hernia has become very much simplified during the past few years, only a few minutes is added to the over-all operating time and our experience with this group of cases has been most satisfactory. When gallstones are present, the gall bladder should also be removed. I have been unable to demonstrate any appreciable increase in morbidity when either or both of these two

TABLE II
LOCATION OF ULCER

Sex	Duodenal	Gastric	Duodenal and Gastric	Marginal	No Ulcer Found	Total
Male	65	22	0	2	4	93
Female	23	15	1	1	2	42
Total	88	37	1	3	6	135

TABLE III
OCCURRENCE OF HEMORRHAGE

Type	No. of Patients
Severe	12
Moderate	17
Mild	22
Total	51

TABLE IV
DURATION OF FOLLOW UP

Time (yrs.)	No. of Patients
6–7	4
5–6	27
4–5	26
3–4	33
2–3	27
1–2	15
Total*	132

* Total stated does not include one operative death (operative mortality 0.74 per cent) and two patients who died later at home.

very important causes of gastrointestinal disturbances have been corrected along with subtotal gastrectomy.

RESULTS

Since all operations in this series were personally performed, we believe the conclusions arrived at are more valuable than had they been done by several visiting surgeons or residents when variations in technic inevitably occur. The execution of technical details is of utmost importance not only in the avoidance of immediate postoperative complications, but also in the construction of the pouch. A new technic should not be suggested to others before a reasonable experience has been obtained.

As Rhode Island is a small state, I have been fortunate in obtaining a 100 per cent follow-up. Except for two patients who were contacted by mail, all have been interviewed repeatedly. This has been most gratifying as cases lost to follow-up may very well represent failures.

In general, I have been impressed with the simplicity of the procedure, with the lack of complications in the postoperative period, and so far, with the end results. There were no cases of obstruction of the afferent or efferent loop, no complications of the duodenal stump, and no cases required operative interference in the postoperative period for any cause with the exception of one wound disruption and one intraperitoneal hemorrhage due to a slipped ligature.

There was one postoperative death (operative mortality 0.7 per cent). This was due to a massive pulmonary embolus on the fifth postoperative day in a fifty-seven year old man who had been having an uneventful convalescence. Two patients died of coronary thrombosis at home at a later date.

Abnormal weight loss occurred in six patients during the first twelve months, but weight stabilized, returned to a reasonable level and has been no problem. All of the patients maintain their present weight on three meals a day, are free of preoperative symptoms, and consider their operations successful. The thin patient with ulcer has the problem of weight loss more frequently. It is in this group that every effort has been made to construct a pouch which will empty slowly and normally and to make certain that not more than two-thirds of the stomach is resected.

One of the most significant observations in the entire group of patients was the almost complete absence of dumping syndrome. Mild symptoms of dumping were reported by only five patients. This syndrome had completely disappeared within a period of three months. I believe that the construction of the gastric pouch that allows food to empty slowly through a lateral stoma is of real importance in eliminating the gravity factor. In the gastric function studies that were made of seventy-one patients, there was a definite correlation between rapid emptying and mild dumping symptoms; there was also a tendency to lose weight during the early postoperative period in this group.

Marginal ulcer developed in three cases (2.2 per cent). Two of these produced bleeding and one perforated. All were in male patients who were forty-one, forty-nine, and fifty-one years of age at the time of their original operations. Recurrence occurred in two of these patients after three years and in one patient after four and a half years. Transthoracic vagotomy

has been performed in all three with complete relief of symptoms. It is of interest that none of these patients had abnormally rapid emptying of their gastric pouches. Therefore, one may conclude that, although a normally functioning pouch has a direct bearing upon weight loss and dumping syndrome, it is not necessarily related to recurrence of ulcer. Some thought has been given to whether or not vagotomy should also be performed with this operation, but so far it has not seemed indicated inasmuch as 97.8 per cent of the entire group are free of symptoms and have not had recurrence of ulcer.

The general well being of patients and their ability to enjoy life is difficult to measure by statistical methods but is more important than a listing of pounds gained or lost, improved acidity levels, or other factors that are commonly quoted as criteria for success or failure. None of the 132 living patients including the three who had recurrence of ulcers, have any regret that they underwent surgery for the relief of their disease. In an over-all survey, making every effort to be objective, I can think of no other group of surgical patients who provide greater satisfaction.

SUMMARY

A new technic for subtotal gastrectomy has been used on a consecutive series of 135 personally performed operations.

Although a longer follow up is necessary, results to date justify the original premise that success depends to a considerable degree upon (1) the construction of a gastric pouch that functions in a normal manner and (2) a more complete utilization of the buffers provided by nature. This can only be achieved by careful attention to certain technical details which have been emphasized.

Postoperative studies of gastric function have been made in seventy-one of the 135 cases. A standard meal to which a small amount of barium had been added was used. This method has been of value in explaining variations in end results that occur after surgery. Forty-nine operations have been performed by this technic since the study discussed herein was completed.

CASE REPORTS

Traumatic Esophagotracheal Fistula

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REVIEW of the medical literature on the subject of esophagotracheal fistulas reveals that the congenital variety has received most attention and that little has been written about the acquired variety of this entity. This latter type is a well known complication of malignant disease of these organs. Most of those not due to malignant disease are due to infection. There is little information about the variety due to penetrating wounds and fistulas due to external violence are quite unusual.

COMMENTS

The first description of an acquired type, based on an autopsy report, was made by McDonnel in 1844 (cited by Abbott [*1*]). Monserratt (cited by Jenkinson) reviewed the world literature on the general subject in 1941 and found 670 cases, of which 222 were congenital, 367 neoplastic, forty-one infections and forty traumatic [*2*]. In 1950 Coleman and Bunch reviewed seventy-five cases of acquired benign fistulas; twenty-six of these were due to infection and eleven were due to traction diverticulum [*3*]. Trauma was the etiologic factor in one-third of these seventy-five cases. More cases of the acquired benign variety were added to Coleman and Bunch's series by Hughes and Fox in 1954 thus bringing the total to eighty-four cases. Thirty-one of these had some type of surgical intervention, four underwent a direct surgical repair, and there were three deaths [*4*]. Volk and Storey reviewed the world literature in 1955 and found seven recorded cases of esophagotracheal fistulas due to nonpenetrating trauma and added one of their own thus bringing the total to eight [*5*]. Five of the eight cases were caused by motor vehicle accidents and three of the five reports stated that the patient was thrown against the steering wheel. In 1957 Lockwood recorded another case, successfully managed, due to nonpenetrating external violence. This patient was also thrown against a steering wheel [*6*]. The patient discussed herein will bring the reported total of acquired, benign cases to eighty-six. This increases the traumatic variety to thirty-four and successful management by direct surgical repair to fourteen. The present case raises the number due to nonpenetrating external violence to ten. In all recorded cases including the present one, the tears have been in a longitudinal direction involving the posterior membranous portion of the tracheobronchial tree and the anterior wall of the esophagus.

Etiology. In seventy-five cases of benign acquired fistulas reviewed by Coleman and Bunch, infection and trauma were the most frequent causes and in that order [*3*]. In the majority of traumatic cases the etiology has usually been some form of direct violence including chemical injuries, perforation by ingestion of foreign bodies, penetrating wounds or perforation during endoscopy. In an extremely small group of patients, an acquired benign esophagotracheal fistula has resulted from indirect violence of nonpenetrating trauma.

Mechanism. It has been suggested that a traction diverticulum antedates the injury in most traumatic cases [*2,3,7,8*]. This diverticulum was probably due to a granulomatous lymph node, which became firmly fixed to the esophagus and the posterior membranous part of trachea or bronchus in the process of healing. Reports of fistulas occurring secondarily to a penetrating injury, foreign body, instrumenta-

tion and the like are fairly common. However, the mechanism in most cases of nonpenetrating external violence remains obscure. It is reasonable to suppose that there has been some fixation, inflammatory in nature, of the esophagus to the posterior surface of trachea and shearing strain or increased intraluminal tension following chest or abdominal injury may produce a tear at the site of this fixation.

CLINICAL FEATURES

In cases in which the tear is large the patient has a sudden choking sensation a few seconds after swallowing fluids. This is immediately followed by a paroxysm of coughing. The patient is usually unaffected by solid food. Food intake may be reduced to a minimum with resulting loss of weight. The appearance of rales in one or both lung fields following the ingestion of liquids (sign of Ono) is described as pathognomonic of esophagotracheal communication. Complications include chronic cough, recurring pneumonia, bronchiectasis and lung abscess. In traumatic cases, symptoms start from the time of injury. The presence of subcutaneous emphysema soon after the injury with coughing after the ingestion of liquids should cause one to suspect the presence of a fistula.

DIAGNOSIS

Fluoroscopy. A swallow of iodized oil should produce a unilateral or bilateral bronchogram depending upon the site of fistula. Iodized oil is preferred to barium. In the case reported herein, however, barium was inadvertently used.

Esophagoscopy and Bronchoscopy. In most instances these procedures will establish the site of the fistula and rule out malignancy as a causative factor or a coincidental finding. In the case reported herein, however, esophagoscopy did not help, possibly due to mucosal folds obscuring the opening. Bronchoscopy may be useful after the patient has been given methylene blue to drink.

TREATMENT

Until recent years most physicians were inclined towards conservative therapy. In Coleman and Bunch's series two-thirds received no specific therapy [3]. Of the fifty-three not surgically treated, sixteen died, four were cured and there were twenty-six unknown results. Of the twenty-two treated by surgery, fifteen were cured, three died and four showed no improvement. Occasionally a very tiny fistula has closed after endoscopic cauterization with silver nitrate [2,3], but direct surgical repair is required in the vast majority of cases. If tuberculosis is present, antituberculosis drug therapy should be prescribed. This medication is likely to render the tuberculous lesion of the esophagus inactive and facilitate surgical correction of the fistula [9]. Most patients require general supportive therapy combined with preliminary jejunostomy or gastrostomy. Direct surgical correction by thoracotomy or cervical approach is the method of choice.

CASE REPORT

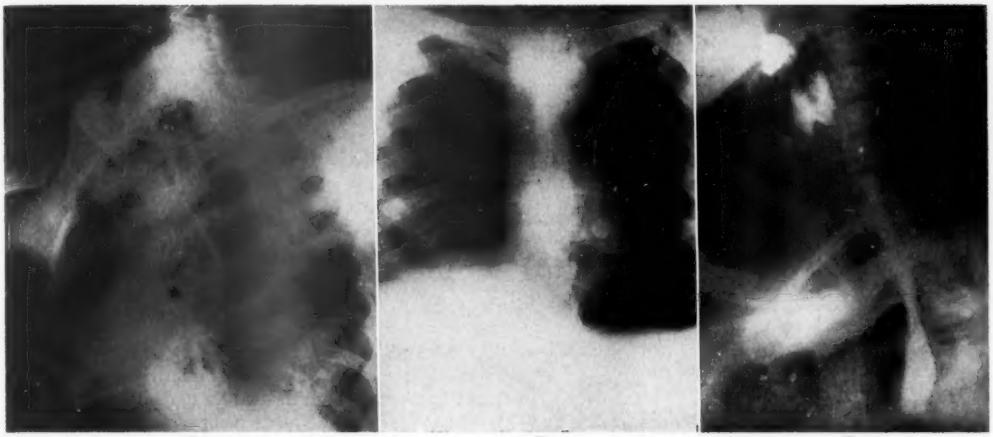
Y. H., a thirty-two year old police constable, was admitted to the hospital on February 1, 1959. An hour before admission the patient became entangled in a wire fence while running to catch a local train. He lost his balance and struck a telegraph pole. His upper chest and lower neck region hit the pole. On physical examination there was marked emphysema of the neck and upper chest. Roentgenogram of the chest was within normal limits. Because of difficulty in swallowing the patient was fed by nasogastric tube for twenty days. After removal of this tube he experienced a choking sensation within a few seconds of swallowing any semisolid or liquid food. This was followed by paroxysms of coughing. He was discharged and advised that he would improve. He was readmitted on March 2, 1959 with the same complaint. Dilatation was performed with no relief and he was discharged after one month.

The patient required admission again on August 31, 1959, because of progressive inanition. On examination he was very anemic, weak and emaciated. The swallowing reflex was normal and neurologic examination revealed no abnormality. Laboratory examination revealed the urine to be normal and the hemoglobin to be 8 gm. per cent. Roentgenogram of the esophagus and stomach with barium showed a quantity of barium to spill out of the cervical esophagus into the trachea a short distance below its origin to produce a partial bilateral bronchogram. (Fig. 1A.)

Esophagoscopy and bronchoscopy failed to reveal the lesion. The diagnosis of acquired traumatic esophagotracheal fistula was made.

Gastrostomy was performed on September 12, 1959, and subsequent feeding improved nutrition considerably. The senior author examined the patient at this stage and he was further prepared for surgery with blood transfusions, dietary supplements and vitamins.

Operation was performed on January 13, 1960. Under endotracheal ether and oxygen anesthesia the cervical esophagus was exposed by an incision along the anterior border of the left sternocleidomastoid muscle. The left lobe of the thyroid was



A B C

FIG. 1. A, bronchogram produced by barium esophageal swallow demonstrating a fistula between cervical esophagus and trachea; site of fistula is indicated by an arrow. B, posteroanterior view; esophageal study one month after operation negative for fistulous tract. C, lateral view; esophageal study with barium one month after operation showed no evidence of leak.

displaced superiorly after dividing the inferior thyroid vessels and middle thyroid vein. The recurrent laryngeal nerve was carefully dissected in its entire cervical extent and preserved. The esophagus and trachea were separated. The esophagus was quite adherent to the trachea over a distance of 1½ inches. The upper limit of this adherence was about 1 inch below the esophagopharyngeal junction. With considerable difficulty the esophagus was dissected and isolated. The fistula was transected, producing an anesthetic leak from the trachea. This was quickly and easily closed by fine interrupted silk sutures in the posterior membranous portion of the trachea. The esophagus was then rotated until the fistulous defect on its anterior surface was visualized. The mucous membrane was approximated with interrupted fine silk sutures and reinforced with a muscular layer of continuous suture of fine silk. The esophagus was returned to its normal position and a corrugated rubber drain was inserted in the operative area. Musculofascial layers were closed with standard technic.

The patient had an uneventful postoperative course. He was maintained on intravenous feeding for four days, and antibiotics were administered for a week. Patient started swallowing semisolids and liquids after a few postoperative days.

An esophagogram made a month after surgery (Fig. 1B and C) demonstrated no esophageal leak. Three months after operation the patient was well and asymptomatic.

SUMMARY

A case of esophagotracheal fistula following nonpenetrating trauma is described. The etiologic factors and mechanisms in traumatic cases are discussed. The essential criteria in diagnosis of this condition are enumerated and its treatment is outlined. The literature on the subject has been briefly reviewed.

Acknowledgment: We are grateful to Dr. Paramanad Yadav, Civil Surgeon, (Kanpur) for allowing us to treat this patient, and to Dr. P. B. L. Saxena for skillful anesthesia.

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Phlegmon as a Complication of Thyroid Cancer

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IN the medical literature there are reports of thyroid cancer developing on the basis of protracted inflammation of the gland of the Riedel type or in the course of subacute inflammation of de Quervain type. However, we did not find any description of cancer of the thyroid complicated by a deep, acute phlegmon of the neck in the literature. This was the reason for publishing our observation.

CASE REPORT

A forty-seven year old woman was brought to the clinic during the emergency duty. Physical examination on admission demonstrated rapidly increasing breathlessness with cyanosis of mucous membranes and ear lobes. Her speech was hoarse and scanty and she answered questions with difficulty. The blood pressure was 140/90 mm. Hg, pulse rate was 120/minute, and the temperature was 37°C. Her skull was symmetrical; the pupils were even, circular, and reacted to light regularly. Her neck was grossly enlarged. On the left side its contours were slightly irregular and there was a protrusion on the anterior surface. The protrusion was greatest near the right supraclavicular pit. The swelling passed upward along the neck and reached as far as the mandibular angle. The skin within the area described showed no inflammatory reaction and was movable. At the site of the eminence some fluctuation was felt. The patient reported an increase in the circumference of the neck which had occurred in the past six weeks, especially on the left side, and difficulties in breathing. Her temperature had remained normal.

Auscultation and percussion of the chest did not produce any pathologic signs. In this way we could exclude the existence of a spontaneous pneumothorax or any other pathologic condition which could account for the patient's symptoms. We were obliged to make an immediate diagnosis because of the patient's condition.

She had been examined by a laryngologist before admission. His diagnosis was a limitation of mobility in the vocal cords and an insignificant stenosis of rima glottidis. The stenosis of the rima glottidis could not be the cause of her present condition.

The patient's breathlessness and cyanosis increased gradually. A puncture test of the right supraclavicular eminence showed purulent content. The patient was operated upon immediately. Under local anesthesia (0.5 per cent novocaine) an incision was made in the right supraclavicular region. The incision produced about 100 ml. of thick, odorless, bloody, purulent content and much necrotic tissue similar in appearance to thyroid tissue.

Manual investigation of the cavity confirmed that it extended toward the spine and behind the clavicle. From the medial side the cavity was limited by a hard cartilaginous infiltration constituting part of the changed thyroid. The entire change appeared to be neoplastic. A section of the tissue was sent for pathologic examination.

After the operation the patient's condition improved for a short time. Her breathlessness decreased, and breathing was deeper and more regular. Cyanosis decreased. This condition lasted for some hours. However, her breathlessness gradually increased and the cyanosis grew more and more serious in spite of the administration of oxygen. We decided to perform a tracheotomy. While cutting the deeper layers of the neck tissues we found about 500 ml. of pus reaching behind the sternum. After stratifying and removing the necrotic tissues of the changed thyroid gland, breathlessness and cyanosis disappeared. As the condition of the patient improved considerably, tracheotomy was discontinued. After insertion of drains, the wound was stitched together with single sutures. The patient was placed in a recumbent position, and cardiac stimulants, antibiotics, and blood were administered.

The following day the patient's condition improved and breathlessness decreased. After some hours the symptoms of increasing breathlessness and cyanosis occurred again and made tracheotomy imperative. After the operation breathing

was normal and cyanosis disappeared entirely. Mucus was removed from the bronchi by suction. Despite this, the general condition of the patient grew worse. The blood pressure decreased to 50 to 60 mm. Hg; the pulse increased to 140/minute. After a few hours the patient died.

Autopsy was performed by Dr. W. Czarnocki at the Institute of Pathological Anatomy of the Medical Academy in Gdańsk. Blood in the ventricles of the heart and the large vessels was not clotted. The heart was dilated especially on the right side. Venostasis of the parenchymatous organs was present as well as neoplastic ulceration of the thyroid. There was neoplastic metastases to the lungs and the lymphatic glands of the mediastinum. Microscopic investigation of the thyroid revealed that the peripheral part of the left lobe was of simple parenchymatous structure. The middle part was white-grey and amorphous. The right lobe and the isthmus were composed of a large, greyish-white, decomposing mass of tissue. Microscopic section of the thyroid tissue revealed anaplastic cancer.

SUMMARY

A rare, deep phlegmon of the neck caused by cancer of the thyroid is described. The case shows the possibility of the formation of phlegmon of the neck in the course of cancer of the thyroid.

Asymptomatic Spontaneous Pneumoperitoneum

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PNEUMOPERITONEUM is a striking radiologic finding that indicates severe intra-abdominal disease and constitutes an urgent surgical emergency. Closure of the offending perforation in the stomach, duodenum or colon must be accomplished as soon as possible to prevent generalized peritonitis, pelvic abscess or intestinal obstruction. Spontaneous pneumoperitoneum of undetermined origin has been reported in the literature and is usually associated with severe symptoms and physical findings that demand exploratory laparotomy [*1,2,5*]. However, complete examination of the gastrointestinal tract at celiotomy has failed to demonstrate a site of perforation in some cases. The origin of air in these cases has been ascribed to a small perforated duodenal ulcer, minute leak from a diverticulum of the colon, rupture of a basilar emphysematous bleb through the diaphragm or insufflation of air by way of the female genital tract [*1,3,5*]. It is unusual to have a patient with spontaneous pneumoperitoneum that is asymptomatic, recurrent and does not require exploratory laparotomy. One such case has been encountered recently during preparation of a patient for pulmonary resection for tuberculosis. This unusual case is presented to illustrate and emphasize conservative management and close observation to avoid unnecessary operation in asymptomatic spontaneous pneumoperitoneum of undetermined origin.

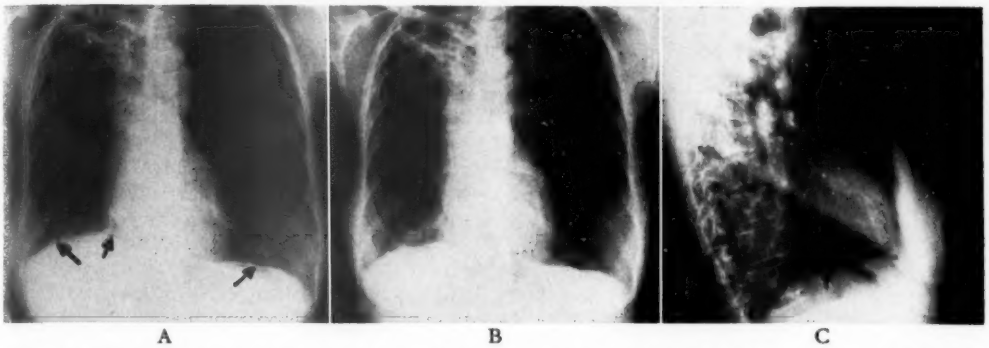
CASE REPORT

H. E., a fifty-three year old Negro housewife, had a two year history of cough, mucopurulent sputum, intermittent fever, night sweats and a 25-pound weight loss. Chest roentgenogram demonstrated a cavity in the right upper lobe surrounded by nodular and linear infiltrations as well as residual fibrotic infiltrations in the right lower lobe. A diagnosis of pulmonary tuberculosis was made. The patient was hospitalized in a sanatorium and treated with bedrest, streptomycin, isoniazid and para-aminosalicylic acid. During this two year period the cavity did not close and sputum cultures remained negative. She was transferred to the Ohio Tuberculosis Hospital on September 25, 1958, for surgical evaluation. The patient stated that she had been pregnant seven times, had six living children and had not menstruated since the age of thirty-nine years.

The patient was a well developed, well nourished Negro woman weighing 104 pounds and in no acute distress. There was increased vocal fremitus and bronchial breath sounds over the base of the right lung posteriorly. The abdomen was protuberant and soft. An upper abdominal midline fascial defect, 3 inches wide and 5 inches long, was present. The tip of the liver, duodenal area and aorta could be palpated through this diastasis recti and no abnormal masses were present in the abdomen. Pelvic examination on admission demonstrated slight enlargement of the uterus consistent with multiple pregnancies. The adnexae were normal and the cervical os was small and stenotic.

Admission hemogram, urinalysis and blood chemistries were within normal limits. Sputum examinations were negative for acid-fast bacilli by smear and culture, and the tuberculin skin test was positive. Pulmonary function studies showed moderate reduction in vital capacity (77 per cent of normal), timed vital capacity (91 per cent of normal), and maximal breathing capacity (50 per cent of normal) compatible with restrictive and obstructive lung impairment. Bronchospirometry indicated that the right lung was performing 30 per cent of the total ventilation and 40 per cent of the total oxygen uptake.

Roentgenograms of the chest on September 26, 1958, showed two cavities measuring 2.5 and 3 cm. in diameter in the retracted right upper lobe. Residual fibrotic infiltrations was seen in the right



A B C

FIG. 1. A, note the retracted right upper lobe which contains a cavity partly overlapped by the clavicle. The right lower lobe is decreased in volume due to fibrotic disease. There is evidence of free air underneath both hemidiaphragms (arrows). B, pulmonary disease is unchanged (January 9, 1959) in comparison with Figure 1A (January 8, 1959). Air in the peritoneal cavity has been absorbed. C, recurrent pneumoperitoneum. Notice the air underneath the right hemidiaphragm (arrow). It is difficult to distinguish the small amount of air below the left hemidiaphragm due to the gastric air bubble and dilated left colon (January 12, 1959).

lower lobe. There was no evidence of a cavity or active infiltration in the left lung. Laminagrams of the right upper and mid-lung fields confirmed the presence of two cavities in the fibrotic right upper lobe. A bronchogram demonstrated bronchiectasis involving the right upper lobe, the superior segment of the right lower lobe, and minor bronchial changes in the medial basilar segment of the right lower lobe. The entire right lower lobe was contracted and the middle lobe was overexpanded compensating for the decrease in volume of both the upper and lower lobes.

The patient was prepared for surgery with a transfusion of 1,000 cc. of whole blood to replace the calculated blood volume deficit, with bronchoscopy to rule out the presence of bronchostenosis and endobronchitis, and with Isuprel® and Alevaire® aerosol to diminish bronchospasm and tracheobronchial secretions. Specific chemotherapy for tuberculosis was given before and after surgery.

A routine monthly roentgenogram of the chest was obtained on January 5, 1959, and showed a slight decrease in size of the cavities in the right upper lobe, but no significant change. Pulmonary resection was planned for January 9, 1959. A preoperative roentgenogram of the chest was taken on January 8, 1959, and demonstrated the pulmonary findings previously reported and free air under both diaphragms. (Fig. 1A.) The patient was interviewed immediately and insisted that she had no abdominal or shoulder pain, nausea, vomiting or other complaints. She had eaten without discomfort, was hungry and had had a bowel movement the day before and on the day the pneumoperitoneum was found. There was no abdominal distention, tenderness, muscle spasm or rebound tenderness. Bowel sounds were normal. The diastasis recti permitted excellent palpation of the upper part of the abdomen and the relaxed lower abdominal musculature permitted thorough bimanual rectovaginal examination. No abnormalities were found during abdominal or pelvic examination. Temperature, pulse and respirations were normal during this day and three succeeding days. Leukocyte count was 5,200 cells per cu. mm. with 56 per cent neutrophils. Urinalysis was within normal limits.

A repeat upright roentgenogram of the chest and abdomen was performed six hours after the first abnormal radiogram and confirmed the presence of free air under the diaphragm. A left lateral decubitus roentgenogram of the abdomen demonstrated that the air shifted over the liver. Surgery was cancelled and a repeat roentgenogram of the chest taken the following day showed that the air had been absorbed. (Fig. 1.B) The pulmonary disease remained unchanged.

Treatment during this time included withholding of food and fluids for twelve hours. In the absence of physical signs the patient was permitted to start taking clear liquids and to progress to a regular diet over the next three days. She was observed closely by repeated abdominal examinations, observations of pulse, temperature, blood pressure, intake and output, and frequency of stools, all of which remained within normal limits.

The patient had no complaints until four days after the previously described pneumoperitoneum had subsided when an upper respiratory infection developed characterized by headache, rhinorrhea, generalized aches, pains, muscle cramps and fever (39.4°C.). She became nauseated, vomited twice and had one liquid stool, but abdominal pain did not develop. Temperature returned to normal in

eight hours. Abdominal and rectovaginal examinations were repeatedly within normal limits except for slight local tenderness when the right costal margin was percussed firmly. Upright roentgenograms of the chest and abdomen demonstrated the recurrence of a slight amount of air under the diaphragm. This was seen better in the right lateral chest roentgenogram underneath the right hemidiaphragm. (Fig. 1C.) Leukocyte count at this time was 12,000 cells per cu. mm. with 77 per cent neutrophils and urinalysis was within normal limits. Repeat leukocyte count eight hours later was 13,200 cells per cu. mm. with 84 per cent neutrophils. The blood count returned to normal the following day. Roentgenographic examination on January 13, 1959, showed no evidence of free air but it was noted again on January 14. Fever was not noted on these two days.

Barium enema was performed on January 13, 1959, and showed no abnormalities. This ruled out the presence of diverticulosis, diverticulitis, pneumatosis cystoides intestinalis, and other cecal or colonic lesions. On January 14 an upper gastrointestinal series and cholecystogram were performed and found to be within normal limits. Intravenous pyelogram was obtained later and showed normally functioning kidneys with lobulation of the right kidney and a bifid right renal pelvis. Repeat roentgenograms of the chest and abdomen on January 16 and 20, and February 3, 1959, failed to show evidence of free air. The pulmonary disease had not changed.

The patient was again prepared for surgery. On February 4 a right upper and lower lobectomy was performed without difficulty. At the time of surgery there were dense pleural adhesions between the lung and diaphragmatic pleura with no evidence of communication through the diaphragm to the peritoneal cavity. The explanation for the origin of the pneumoperitoneum could not be attributed to the pulmonary disease from this dissection. The pathologic report of the tissue removed was chronic fibroid and fibrocaseous pulmonary tuberculosis with a filled cavity, bronchiectasis and extensive nodular disease throughout both the upper and lower lobes.

The patient did well postoperatively despite an atelectasis treated successfully with expectorants and vigorous coughing. Repeat roentgenograms of the chest postoperatively failed to show recurrence of the pneumoperitoneum nor did the patient have any complaints referable to the abdomen. Prior to discharge repeat barium enema and upper gastrointestinal series were obtained and no abnormalities found.

COMMENTS

Pneumoperitoneum is an alarming radiologic finding that usually indicates the presence of a ruptured viscus complicating a pre-existing intra-abdominal lesion. The common causes of symptomatic pneumoperitoneum include perforated duodenal or gastric ulcer, ruptured gangrenous appendicitis, leaking diverticulum of the colon, or trauma producing rupture of the stomach, small bowel or colon. Other less common causes are rupture of a Meckel's diverticulum, perforation from ulcerative or amebic colitis, leakage of air from subserosal blebs in pneumatosis cystoides intestinalis, or perforation of pulmonary emphysematous blebs through the diaphragm into the peritoneal cavity. In each of these diseases pneumoperitoneum is accompanied by profound symptoms and physical signs of generalized peritonitis. There is little doubt that immediate exploratory laparotomy and surgical correction are indicated.

Pneumoperitoneum, on the other hand, may be a complication of endoscopic examination such as sigmoidoscopy or cystoscopy, perforation of distended bowel during aspiration of fluid by paracentesis, or low thoracentesis in which the diaphragm is perforated and the peritoneal cavity entered. These procedures may be followed by peritonitis requiring surgical intervention and correction. On the other hand, air may be introduced into the peritoneal space for diagnostic or therapeutic reasons and is of no concern in this discussion.

Spontaneous pneumoperitoneum of undetermined origin has been explained by various authors as the passage of air into the peritoneal cavity through the female genital tract, usually in the immediate postpartum period [*1,3,5*]. Reports of pneumoperitoneum in patients following postpartum knee-chest exercises have appeared [*3*], and one case of fatal air embolism has been reported in which air entered a patent uterine vein [*4*].

The explanation for pneumoperitoneum in the case presented herein remains obscure. When the patient was questioned thoroughly, she stated that she had not taken a douche, assumed the knee-chest position, had coughing paroxysms with sudden inhalation, or had pelvic instrumentation prior to development of the pneumoperitoneum. Repeated questioning and physical examinations failed to disclose symptoms or findings that might explain the origin of the air. Complete roentgenographic examination of the gastrointestinal tract on two occasions failed to demonstrate a pathologic lesion that might account for the presence

of air in the peritoneal space. The patient was postmenopausal and pelvic examination demonstrated a stenotic cervical os, slightly enlarged uterus and a patulous vagina. In view of the absence of other findings it must be assumed that the origin of the pneumoperitoneum in this patient was via the genital tract.

When free air is found under the diaphragm in symptomatic spontaneous pneumoperitoneum, immediate exploratory laparotomy is indicated. In this patient neither signs of peritonitis nor symptoms suggesting involvement of the gastrointestinal tract were present and a conservative approach was followed. The abdomen was examined repeatedly to be sure the pneumoperitoneum did not progress and signs of peritonitis did not develop. Radiologic examination completely excluded the common lesions as a possible source of pneumoperitoneum, yet the pneumoperitoneum recurred, subsided and has not recurred.

Spontaneous pneumoperitoneum via the genital tract not in the postpartum state is rare. In reported cases exploratory laparotomy has been performed because symptoms of peritonitis were present in addition to the spontaneous pneumoperitoneum. In the case presented in this report exploratory laparotomy was not performed because signs of peritonitis did not develop despite the finding of free air under the diaphragm. She was followed up in the hospital, convalescing from her pulmonary tuberculosis, for five months after the finding of spontaneous pneumoperitoneum and had no recurrence or complication of this finding.

CONCLUSIONS

1. A case in which a fifty-three year old woman had asymptomatic spontaneous pneumoperitoneum fourteen years following menopause is presented.

2. Exploratory celiotomy was not performed since the patient was asymptomatic.

3. Repeated and careful examinations of the abdomen, vital signs and leukocyte count must be performed if conservative management is elected.

4. Complete radiologic examination of the gastrointestinal tract is necessary to eliminate an unrecognized lesion that might explain the origin of the spontaneous pneumoperitoneum.

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Tumor of the Cecum with Cystic Fibrosis of the Pancreas

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CYSTIC fibrosis of the pancreas is a relatively rare hereditary and possibly familial disease in which the pancreas fails to secrete the enzymes necessary for proper breakdown of proteins and fats into the duodenum. It was thought earlier to be a disease affecting all of the mucous glands of the body, but recently involvement of other exocrine glands including sweat and salivary glands have been found [1].

The usual complications of this disease include intestinal obstruction such as meconium ileus in the neonatal period, malabsorption and nutritional problems, and pulmonary problems. Recently portal hypertension secondary to diffuse biliary cirrhosis has been seen in association with cystic fibrosis of the pancreas [2]. Most of these have been in older children from four to twelve years of age, and there have been a few cases reported of massive bleeding from esophageal varices. Survival without surgery is nil; the results of portal-systemic venous shunting procedures have been encouraging in a few cases [3].

In patients with cystic fibrosis of the pancreas, the obstructive phenomena affecting the intestinal tract usually occur in the immediate neonatal period and are characterized by acute obstruction of the small bowel due to inspissation of thick, tenacious meconium which usually occurs in the terminal ileum. Meconium ileus accounts for approximately 15 per cent of all neonatal bowel obstructions. Until recently this situation has been universally fatal but enterostomy and/or enterostomy with repeated irrigations of the meconium-filled bowel with saline solutions of pancreatin have been associated with survival in about 80 per cent of such cases [4].

Even if the child survives the neonatal period he may still develop intestinal obstruction. Improper diet can be responsible for severe fecal impaction and even obstruction. We believe that another condition can occur when there are signs of a mass in the large bowel.

CASE REPORT

An eighteen months old female child was first admitted to St. Vincent's Hospital on December 29, 1955 with a painless mass in the right lower quadrant. The history was obtained from the mother.

About a month before admission a painless mass was found in the right lower quadrant by the local physician. The child had had no symptoms. The appetite had been good, weight gain had been normal, and bowel movements were regular without blood. There had been no vomiting and the child had behaved normally. Weight at birth was 6 pounds and 10 ounces; at one year of age the weight was 19 pounds.

The patient had had a cough which was productive of white sputum from birth until August of 1955. There had never been any blood in the sputum. Since August the cough had been nonproductive and had been treated with tetracycline for fibrocystic disease of the lung.

The child had been normally active, said many words, and walked at nine months. A younger sibling had died of cystic fibrosis at the age of three months.

Delivery was uncomplicated. Patient had been immunized against diphtheria, pertussis, tetanus and smallpox.

Physical examination revealed no abnormalities except for a non-tender, freely movable, oval to spherical (2 by 3 cm.) mass in the right lower quadrant. There was a hemangioma (2 by 4 cm.) over the left lower anterior rib cage.

Intravenous pyelograms revealed normal kidney function and contour. Barium enema revealed an ill-defined mass in the cecum. (Fig. 1.) Roentgenograms of the chest revealed patchy consolidation throughout the right, middle and lower lobe. Hemoglobin was 13.5 gm. per cent, erythrocyte count

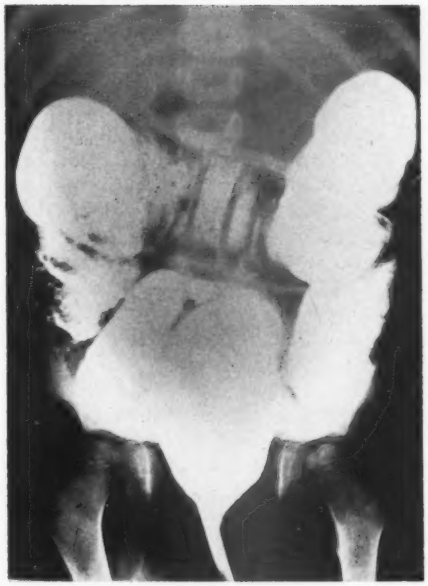

FIG. 1.

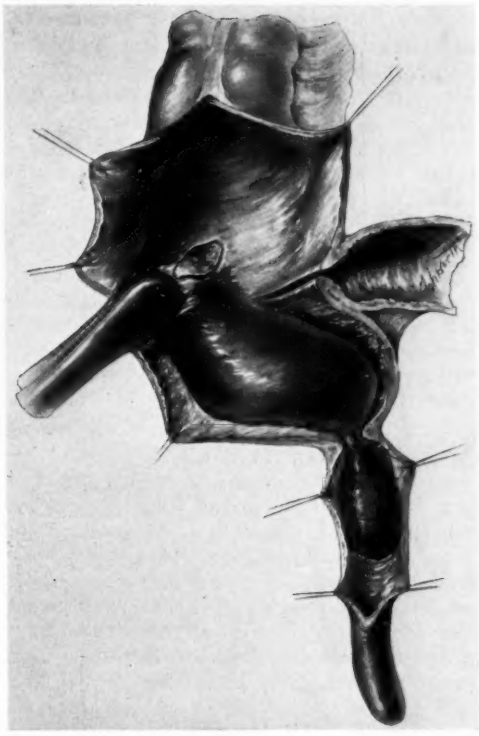

FIG. 2.

was 4,940,000 and leukocyte count was 8,900 with a normal differential.

The patient was treated with intensive antibiotic therapy for a period of ten days without change in symptoms or in the appearance of the patchy consolidation. Laparotomy was then performed. The preoperative diagnosis was mucocele of the appendix. At operation a lower right rectus incision was made. Exploration of the abdomen revealed no palpable pathology except in the right lower quadrant. There was a mass (2 by 3 cm.) in the cecum which could be molded like feces but could not be moved along the bowel. When the cecum was opened, a pliable, yellowish, waxy mass was found. It was so densely adherent to the mucosa of the cecum that stripping it caused punctate bleeding of the mucosa. (Fig. 2.) In some areas the mucosa was actually stripped away with the mass, which extended into the lumen of the appendix. The mass was carefully separated from the mucosa and removed, and an appendectomy was performed because the lumen of the appendix was obstructed by the material. The cecum was then closed in layers and the abdominal incision was closed. The patient made an uneventful recovery. The pathologic report was "inspissated fecal material."

The child continued to have pulmonary symptoms with productive cough and progressive changes in roentgenograms of the chest. The condition gradually grew worse and she died at the age of three and a half years of chronic purulent pulmonary disease.

COMMENTS

Extensive reports of early obstruction of the small bowel associated with cystic fibrosis of the pancreas manifested as meconium ileus are available.

Early obstruction of the large bowel does occur in the neonatal period in a condition which has recently been referred to as the "meconium plug syndrome" [5]. However, only the initial plug of meconium may be defective of tryptic activity and it should be emphasized that this condition bears no etiologic relationship whatever to meconium ileus or to cystic fibrosis of the pancreas. There is, however, only an occasional reference in the literature to delayed obstruction of the small bowel as a complication in patients with cystic fibrosis of the pancreas who survive the neonatal period.

Delayed formation of a mass in the large bowel must be a relatively rare condition or at least it is rarely reported. The presence of palpable, modeling-clay–like masses along the

course of the large bowel is well illustrated by the case reported herein. The fact that these soft, cast-like, waxy collections were so tightly adherent that the wall of the cecum was denuded of mucosa when they were removed would explain why repeated, thorough enemas failed to dislodge them. No attempt was made to use other agents in the enema fluid, such as hydrogen peroxide or pancreatic solution.

This case illustrates an unusual example of a surgical problem that may arise in children with cystic fibrosis of the pancreas. We believe that any child who has this disease is a candidate for delayed partial obstruction of the large bowel if these modeling-clay–like masses accumulate. It is possible that these adherent masses can produce symptoms of intussusception. The possibility of polyps or tumors of the large bowel could not be excluded by barium contrast media in this case. Therefore, laparotomy and cecotomy were necessary to establish the diagnosis.

Recent electrophoretic studies in patients who have meconium ileus show that their meconium contains proteins identical with serum proteins. It is postulated that in the absence of normal proteolytic activity the small bowel of these patients becomes the site for interaction of these serum-like proteins with the mucopolysaccharides in the intestine that go into the formation of normal meconium. The result is the formation of the highly viscous obstructive meconium seen in patients with meconium ileus [6]. Whether the masses seen in the case presented were residue of an undiagnosed meconium ileus in the neonatal period is unknown. We doubt this, however, because of their size.

SUMMARY

1. An unusual case is presented of a child with cystic fibrosis of the pancreas in whom palpable, modeling-clay–like masses developed in the cecum at the age of eighteen months.

2. In this case it was impossible to rule out intraluminal tumor masses or polyps in the large bowel preoperatively by the usual diagnostic methods.

3. A history of cystic fibrosis of the pancreas should be an important consideration in the evaluation of any case of obstruction of the large bowel that occurs after the neonatal period.

4. It is suggested that perhaps repeated enemas containing dilute saline solutions of pancreatin would have caused dissolution of these large bowel masses and, therefore, eliminated the necessity of surgical intervention.

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Diffuse Idiopathic Fibrosis

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DENSE COLLAGENOUS hyalinized connective tissue may produce lesions which simulate neoplastic disease both in the gross appearance and the apparent metastatic nature of the distribution. The following case report is an unusual example of idiopathic fibrosis involving both the thoracic and abdominal cavities with extension into the pelvis.

There have been a number of cases reported in the literature in the past hundred years describing a variety of conditions due to idiopathic fibrosis. The earliest reports according to Barrett [3] dealt with unexplained superior vena caval obstruction caused by fibrous tissue. These reports are variously credited to Hunter in 1757 and Hallet in 1848. Ochsner and Dixon [7] in 1936 noted twenty-eight of 120 cases of superior vena caval obstruction which they attributed to mediastinal fibrosis; only five of these were idiopathic.

There have been several reports in the urologic literature in the past ten years of a new clinical entity called periureteric fibrosis or idiopathic retroperitoneal fibrosis which was first described by Ormond [8] in 1948. In his review of the subject in 1958, Hackett [6] concluded that the condition was limited by the renal fascia to a space bounded by the diaphragm, brim of the pelvis and lines 1 cm. lateral to the ureters on either side.

In 1946, Tubbs [12] reported the case of a twenty-five year old man with typical idiopathic mediastinal fibrosis revealed at thoracotomy. Periureteric fibrosis with stenosis of the inferior vena cava was found at autopsy. The present case appears to be the second with involvement above and below the diaphragm.

CASE REPORT

A thirty-nine year old white plant manager was first admitted to the hospital in 1951 because of a nine year history of recurrent hemoptysis associated with attacks of bronchitis. Hemoptysis and loss of weight had begun when the patient had a cold and cough which had lasted for several weeks. Chest x-rays had revealed dormant tuberculosis. Following a stay in Arizona and the removal of infected nasal polyps, the cough had disappeared and the patient had gained weight and strength. During three years of service in the Army he had noted dyspnea after undue effort.

Hemoptyses had become more profuse for the three years prior to admission and had been associated with attacks of bronchitis occurring once or twice each winter. Repeated sputa had been negative for tuberculosis but no tuberculin tests had been performed.

One year prior to admission the patient had had a one week episode of epigastric pain radiating around the right costal margin associated with belching, constipation, light stools and jaundice. Xanthomatous deposits about the left eye had been present for an unknown period. He had not indulged in smoking or drinking.

Physical examination of the heart and lungs revealed no abnormalities. The liver was not tender but was enlarged to 3 cm. beneath the right costal margin.

Bronchoscopy revealed prominent bronchial vessels with active bleeding from both main stem bronchi. Roentgenogram of the chest showed haziness of the lower half of the left lung field. There was nonvisualization of the gallbladder, a bromsulfathalein retention of 35 per cent and a total bilirubin of 2.3 mg. per cent. Results of urine examination was within normal limits. The white blood cell count was only 3,600 per cu. mm. He was discharged without treatment.

The patient was readmitted in January 1957 with bandlike pain in the upper abdomen radiating into the back on both sides. The pain had begun two months previous with nausea, vomiting and diarrhea. It was intensified by fried food and occasionally by alcohol. Examination was the same as during the previous admission. A chest x-ray was interpreted as thickened pleura over the left lower lung field with some calcification. Barium enema (Fig. 1) was normal but showed a large spleen. Studies of the upper gastrointestinal tract (Fig. 2)

FIG. 1. Normal barium enema showing splenic flexure of the colon displaced by a big spleen.

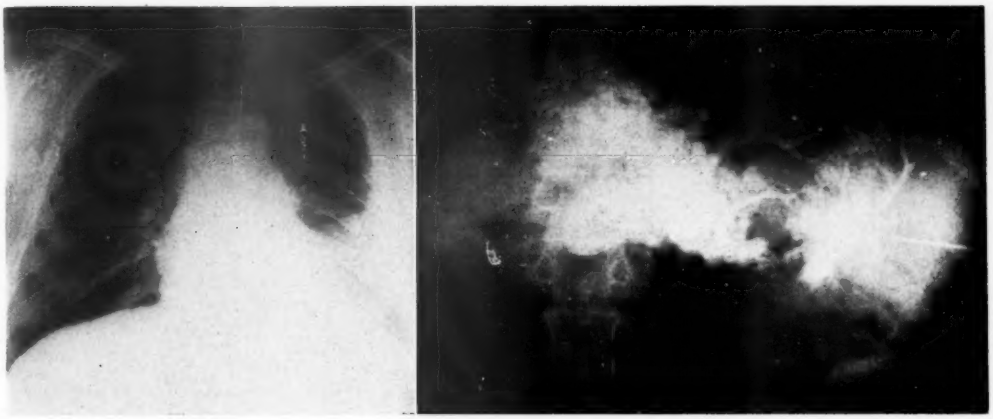
FIG. 2. Barium swallow with esophageal varices extending above aortic arch.

revealed large esophageal varices and a fusiform soft tissue mass around the lower esophagus. Electrocardiogram was normal. There was 40 per cent bromsulfathalein retention with a negative cephalin flocculation test. The patient was discharged on an ulcer diet.

The last admission, in April 1958, was for active hemoptysis and/or hematemesis of twenty-four hours' duration occurring after slight exertion. There was no pleuritic pain, angina, orthopnea, edema of the ankles or bleeding tendency. Examination revealed decreased breath sounds over the lower left lung with the left side of the diaphragm in a relatively fixed position. The liver and spleen were enlarged and there were spider nevi over the chest and upper arms. Electrocardiogram revealed no abnormalities. Cephalin flocculation was 4 plus, but the bromsulfathalein retention had decreased to 10 per cent. Blood urea nitrogen was within normal limits as was the urine. Chest x-ray (Fig. 3A) was unchanged.

A percutaneous splenoportagram (Fig. 3B) showed no splenic or portal vein with varices in the region of the cardia of the stomach and the lower end of the esophagus. Left thoracoabdominal laparotomy disclosed dilated subcutaneous veins up to 6 mm. in diameter over the left thoracic wall and a woody thickened pleura. There was no free pleural space; the lung was adherent to the diaphragm and lateral thoracic wall by adhesions containing numerous large vessels. There was no ascites. The spleen was greatly enlarged and bound to a hard irregular retroperitoneal mass which appeared to encase the left kidney and to extend behind the pancreas to the porta of the liver. The liver did not appear cirrhotic but contained a spherical yellow stony hard mass at the central end of the round ligament. Frozen sections of this mass showed only hyalinized connective tissue. The mass could be felt extending into both lobes of the liver under a thin layer of tissue which appeared normal. Portal pressure measured in an omental vein was 420 mm. of saline. As no vascular shunt was available, the operation was terminated with a diagnosis of probable inoperable malignant tumor.

On the sixth postoperative day, midabdominal cramps, abdominal tenderness and a mass in the right lower abdomen developed. Reoperation dis-



3A 3B

FIG. 3. A, chest film revealing haziness of lower half of the left lung field. B, percutaneous splenoportagram showing varices in region of cardia of stomach but no splenic or portal vein.

closed gangrenous small bowel with the entire root of the mesentery involved in the same hard tissue. The patient died three days later.

At autopsy, there were multiple venous occlusions above and below the diaphragm because of concentric rings of hyalinized connective tissue within the vessels. There was a confluent mass of dense connective tissue in the upper abdomen, mediastinum and left pleural cavity as well as isolated masses of this same tissue in various widely separated places.* (Fig. 4.)

The portal vein and all its intrahepatic branches were entirely occluded. There were also small isolated nodules of connective tissue in the liver parenchyma. The splenic vein and all of its hilar branches were obliterated. The superior mesenteric vein and tributaries extending almost to the cecum were solidly organized. The inferior mesenteric vein was markedly narrowed. The arteries corresponding to these veins were surrounded by solid fibrous connective tissue but were not constricted. The common bile duct was also completely surrounded but not obstructed.

The right renal vein was replaced by fibrous connective tissue from its origin in the kidney parenchyma to within 1 cm. of the vena cava. The left renal vein was markedly narrowed but the kidney was not invaded except for a 0.5 cm. nodule at the lower pole. The renal capsule was intact but the perirenal tissue was largely replaced by hyalinized connective tissue. The ureters were surrounded but not obstructed.

The inferior vena cava was not narrowed or involved although completely surrounded by the same tissue.

There was a spherical isolated mass of hyalinized connective tissue 4 cm. in diameter in the region of the cecum and another similar mass measuring 3.5 by 2.5 by 0.4 cm. between the rectum and the sacrum.

The pleura of the left lung including its diaphragmatic portion and extending about halfway to the apex was thickened to 0.8 cm. by chitenous hyalinized connective tissue. The muscle of the diaphragm was also invaded.

The left inferior pulmonary vein and its branches were completely occluded for about one-third of the way to the periphery. The left superior pulmonary vein was narrowed to a 2 mm. lumen. The right superior and inferior pulmonary veins were narrowed to a lumen of 1.5 mm., but the occlusion did not extend into the lung parenchyma. The azygos

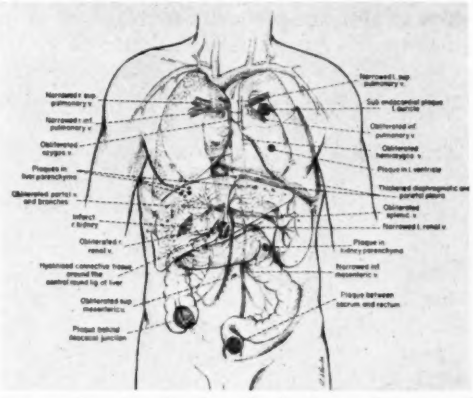
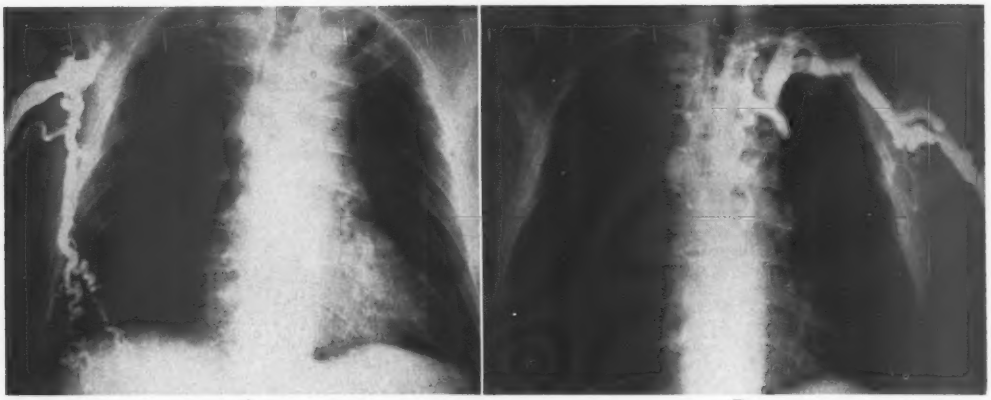


FIG. 4. Drawing showing distribution and extent of areas of fibrosis.

* A detailed pathologic study of this case will be published by Drs. Alan Moritz and George R. Abbott.



5A 5B

FIG. 5. A, venogram of right arm with block in axillary vein and enlarged thoracoabdominal collateral circulation. B, venogram of left arm showing block in left innominate vein and collateral by way of intercostal, accessory hemiazygos and azygos veins. Permission to publish these venograms has been granted by Dr. Henry Fertig. They are not from the case presented.

and hemiazygos veins were totally obliterated, however, the superior vena cava was not involved. There was a mass of yellow hyalinized connective tissue 2 cm. in diameter in the wall of the left atrium lying just beneath the endocardium. There was a similar isolated mass 1 cm. in diameter in the myocardium of the left ventricle.

There was no evidence in multiple sections from all of these areas of any specific etiologic factor for these findings.

COMMENTS

It is obvious from this case report that surgery could offer very little toward the relief of serious but not totally disabling symptoms. Awareness of the entity of idiopathic fibrosis and means for its diagnosis are, therefore, of prime importance as the disease is usually self-limited and surgery is rarely helpful.

The diagnosis of idiopathic mediastinal fibrosis with superior caval obstruction is greatly facilitated by obtaining venograms of both arms. These frequently will localize the site of the block and indicate its extent through study of the dilated collateral circulation. (Fig. 5A and B.)

Allansmith [1] has described a tourniquet test for the differentiation of superior caval block above and distal to the azygos vein. A tourniquet is applied to the chest, constricting the superficial thoracoabdominal vessels. If the venous pressure in the arms rises with inspiration the block is distal to and involves the azygos vein.

Costal intraosseous venography described by Schobinger, Cooper and Rousselot [11] gives a more definitive evaluation of the collateral circulation because the contrast media fills the intercostal, hemiazygos and azygos veins in turn. Under local anesthesia, a 16 gauge Rosenthal bone marrow needle is introduced with the stylet in place into the medullary cavity of the left ninth or tenth rib in the midaxillary line. Correct positioning is verified by the aspiration of blood and bone marrow and 2 cc. of 2 per cent procaine are injected. Twenty cubic centimeters of 50 per cent Hypaque® Sodium (sodium 3,5-diacetamido-2,4,6-triiodobenzoate) are then injected within five seconds. One film is exposed during the end of the injection. This procedure can be accomplished on an ambulatory basis. Unfortunately, it was not employed in the case under discussion. If it had been, it should have revealed the extensive superficial collateral circulation in the chest wall and the azygos and hemiazygos block.

The diagnosis of periureteric or idiopathic retroperitoneal fibrosis is suggested by symptoms such as pain in the lumbar region which indicate a block of the ureters. Elevated levels of urea in the blood in Hackett's case [6] may be present with edema of the legs if the inferior vena cava is involved. As pointed out by Raper [9], ureteral catheters may pass up a partially blocked ureter without detecting the block but retrograde pyelograms usually reveal some degree of hydronephrosis. In the present case

there were no urinary symptoms and no evidence of renal failure in spite of the complete occlusion of the right renal vein with an infarct in that kidney and the marked narrowing of the left renal vein. The lack of symptoms was probably due to the fact that the ureters were not obstructed in spite of being surrounded by fibrous connective tissue. A definite diagnosis in either mediastinal or retroperitoneal fibrosis can be made only after exploration and biopsy.

The pathways of venous collateral circulation with superior vena caval block above and including the azygos vein have been thoroughly worked out. Carlson [4] demonstrated that dogs would not tolerate a sudden occlusion of the superior cava and azygos vein although they would survive if the vessels were ligated separately in two stages. He worked out two types of collateral circulation depending upon whether or not the azygos vein was patent. The superficial plexus of veins of the thorax and abdomen connecting the upper and lower extremities were common to both types as was the internal mammary, superior and inferior epigastric plexus connecting the innominates to the external iliacs. In the block above the azygos vein, the superior intercostal veins communicating with the accessory hemiazygos and azygos veins were the chief pathways of venous return. In the lower type of block including the azygos vein, the vertebral plexus including the internal vertebral, intervertebral, intercostal and lumbar veins emptying into the inferior vena cava was the most important means of collateral circulation. The deep veins of the back were not prominent in either type of block.

The problem of collateral circulation in the present case is unusual in that neither the superior nor inferior vena cava was obstructed. Instead, the venous return from three main organ systems was either completely blocked or very seriously impaired. The portal, splenic and most of the superior mesenteric vein were totally occluded without impairment of their corresponding arteries. This produced the plexus of varices in the region of the cardia of the stomach continuing into esophageal varices which extended above the arch of the aorta as their normal run-off through the hemiazygos and azygos veins was also blocked. Retroperitoneal attachments to the spleen were numerous but relatively small. Normal collateral circulation from the capsule of the spleen to the left side of the diaphragm was blocked by involvement of the diaphragm and the pleura of the left lung. The subperitoneal veins in the abdominal wall were large and tortuous.

Venous return from the kidneys must have been accomplished through the retroperitoneal plexus of small veins, adrenal veins and lumbar veins into the inferior vena cava. There were no injection studies; and postmortem evaluation of the size of vessels in this area was difficult.

Venous return from the lungs was impaired, as evidenced by dyspnea on effort for at least fourteen years before the patient's death. Collateral vessels known to have been enlarged were the dilated and tortuous bronchial veins responsible for the hemoptysis, and numerous veins of moderate size running from the lung parenchyma to the chest wall in the many pleural adhesions.

In spite of the absence of effective medical treatment for idiopathic fibrosis, surgery should rarely be employed if a presumptive diagnosis can be made. The disease tends to be self-limiting, leaving unpleasant but rarely totally disabling symptoms. Beneficial results from surgery depend upon the possibility of remedying mechanical problems produced by the fibrosis. Removal of the fibrous mass is rarely possible without destruction of vital vascular structures, although at times it is possible to free the ureters of constriction. Blood vessel grafts to bridge areas of obliteration have been utilized by Gerbode [5], Scannell [10] and others, but these grafts frequently thrombose or become obliterated by the same fibrotic process. Exploration with biopsy as was done in the case reported here entails a considerable mortality due to intravascular clotting. With such extensive destruction of vessels, there is little possibility for surgery to improve on what has already been accomplished by natural collateral circulation.

SUMMARY

A case of diffuse idiopathic fibrosis involving both mediastinal and retroperitoneal areas is described. This is apparently the second such case reported involving structures above and below the diaphragm. Diagnosis of the condition is helped by obtaining appropriate venograms. The technic of intraosseous venography described by Schobinger, Cooper and Rousselot [11] should permit a definitive evaluation of mediastinal collateral circulation. Medical treatment of this condition is ineffective. Surgical

treatment is seldom helpful and carries a high mortality because of intravascular clotting. Naturally developing collateral circulation and a tendency for the disease to be self-limited will usually permit the untreated patient to lead a handicapped life of relatively normal duration.

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Carcinoma of the Thyroid Occurring in a Diffuse Toxic Goiter

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THE rarity of carcinoma of the thyroid in the presence of diffuse toxic goiter has been well established in recent reviews in the literature. In 1948 Pemberton and Black [*1*] showed that in a collected series of 1,210 patients with carcinoma of the thyroid gland this association occurred in only 1.75 per cent. Conversely, by collecting previously recorded cases, Sokal [*2*] found that cancer occurred in only 0.15 per cent of 13,868 patients whose thyroid gland had been surgically removed because of diffuse toxic goiter. However, since this extensive review of the subject, only isolated cases have been reported in the literature [*3–6*]. Recently, Sawyer and Alfonso [*7*] reviewed sixty-five cases of carcinoma of the thyroid gland in patients who have been surgically treated at this institution since 1946. During this same period, 249 thyroid glands were removed because of diffuse toxic goiter and all cases were confirmed by histologic examination of the thyroid tissue removed. A recent case is reported herein in which carcinoma occurred in a diffuse toxic goiter. A second case was excluded because the consulting pathologists did not concur that carcinoma was present in a thyroid showing diffuse hyperplasia. Thus one of the sixty-five carcinomas (1.54 per cent) was associated with diffuse hyperplasia of the thyroid and one of 249 cases of diffuse hyperplasia (0.40 per cent) showed carcinoma. These statistics are comparable to those of Pemberton and Black, and Sokal.

CASE REPORT

A seventeen year old white married woman returned for a routine six-weeks postpartum examination on October 27, 1958, with the complaints of progressive nervousness, sweating, shakiness, fatigue, fullness in the neck and increased appetite. She had gained 24 pounds during pregnancy; however, her weight at this examination was 109 pounds.

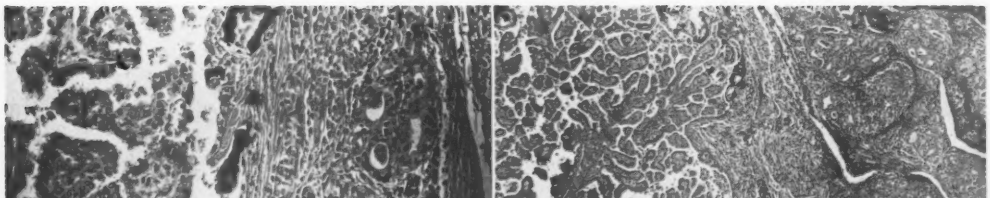
Examination revealed an apprehensive and nervous patient. Blood pressure was 144/84 mm. Hg, and radial pulse was 88 per minute and regular. A fine tremor of the fingers was noted when the arms were outstretched. Palpation of the neck revealed a diffuse bilateral enlargement of the thyroid gland with no evidence of nodulation or cervical adenopathy. There was no evidence of exophthalmos. The remaining physical examination was noncontributory. Serum protein-bound iodine determination was 12.5 μg. per cent (4 to 8 μg. per cent is normal for this laboratory).

Routine presurgical treatment with Lugol's solution, a high caloric diet and rest were immediately instituted. The patient noted a dramatic relief of toxic symptoms and her weight was 120 pounds upon admission to the hospital six weeks later. Blood pressure was 120/80 mm. Hg, and radial pulse was 70 per minute and regular. There was no evidence of nervousness or tremor but the thyroid was still palpable.

On admission routine hemanalysis, urinalysis and roentgenograms of the chest revealed no abnormalities. On December 11, 1958, bilateral, subtotal thyroidectomy was performed without complication.

Gross pathologic examination revealed the following: the right and left lobes of the thyroid totaled 39 gm. The right lobe measured 6 by 3.5 by 2.5 cm., and the left lobe measured 5 by 3.5 by 2.5 cm. Each lobe was firm with a smooth red-gray capsule. Multiple thin sections revealed a finely lobular, tan to red-brown, somewhat meaty cut surface in which the colloid content was grossly diminished. The cut surface was homogeneous throughout with no gross evidence of nodules, although minute gray stippled areas were diffusely dispersed.

Microscopically, the irregular and variably sized follicles were empty or contained poorly staining colloid which showed characteristic peripheral vacuolation. The epithelium was tall and columnar with stratification and papillary infolding of the



1A 1B

FIG. 1. A, section of thyroid gland showing well differentiated papillary carcinoma to the left and diffuse hyperplasia with follicular lymphocytic infiltration to the right. Note apparent invasion through the thin fibrous wall near the top of the figure. (Hematoxylin and eosin stain, original magnification × 50.) B, high power, view of Figure 1A showing calcified psammoma bodies at the fibrous junction of the papillary carcinoma and hyperplastic thyroid tissue. (Hematoxylin and eosin stain, original magnification × 200.)

epithelial cells in some follicles. A few mitotic figures were noted within this hyperplastic epithelium. The characteristic involution usually seen following iodine therapy was observed in only a few focal areas. There was some increase in the interstitial fibrous tissue which also showed both diffuse and follicular lymphocytic infiltration. In one small focal area in a section from the right lobe and demarcated from the adjacent hyperplastic thyroid parenchyma by a thin fibrous wall, there was a cancerous proliferation of the glandular epithelium with a characteristic pattern of papillary carcinoma. (Figs. 1A and B.) The fibrous wall was invaded on one side. Characteristic psammoma bodies were numerous throughout this cancerous growth. Since this small cancer was not suspected from gross examination, repeat sections of the wet specimen of each lobe were made. Two similar areas of papillary carcinoma were found within the right lobe adjacent to the original one. Serial sections of the left lobe revealed no microscopic evidence of cancer.

COMMENTS

There was strong clinical evidence of thyrotoxicosis in this case and it differed from the classical case of Graves' disease only in the absence of ocular signs. The clinical diagnosis was supported by the elevated protein-bound iodine and later by the rapid remission of toxic signs and symptoms when iodine therapy was administered. The diffusely enlarged gland was easily removed and there was no evidence of cervical adenopathy.

The fact that carcinoma was not suspected clinically in this case is not surprising since none of the twenty-two cases reported by Pemberton and Black [*1*] had been suspected. In the majority of their cases, as in the present case, the carcinoma was not recognized as such even on gross examination of the surgical specimen. Their conclusion was that in many cases such lesions can be recognized only if all grossly visible nodules, however small, are sectioned and examined microscopically. Since most patients are treated preoperatively with iodine, small nodular areas of involution may obscure the presence of small true adenomas and may, therefore, escape the eye of the prosector. In a later report by Beahrs, Pemberton and Black [*8*], fourteen carcinomas were found in 3,029 patients whose thyroid glands showed diffuse hyperplasia. Almost all these cancers were small, sclerosing papillary growths which showed little tendency to recur or metastasize. It is evident, therefore, that for the diagnosis to be made before surgical intervention there must be a rare, rapidly growing cancer or evidence of metastasis with clinical diffuse toxic goiter.

Boulet *et al.* [*3*] report a case in which a diffuse toxic goiter grew rapidly following treatment with antithyroid drugs. Pathologic examination of the surgical specimen revealed carcinoma. They concluded that antithyroid drugs may augment a pre-existent cancer and that the prognosis is guarded in any case in which a diffuse toxic goiter begins to grow rapidly after treatment with antithyroid drugs.

In the majority of cases, however, cancers associated with diffuse hyperplasia of the thyroid will be small and probably need not be seriously considered, especially in the case of papillary carcinoma.

The patient's age is of some interest in this case although carcinoma of the thyroid gland is not rare in young people. Duffy and Fitzgerald [9] found that twenty-eight of 403 (6.5 per cent) patients with carcinoma of the thyroid gland were under eighteen years of age. In the following year, Horn and Ravdin [10] found that twenty-two of 159 (13.8 per cent) patients with carcinomas of the thyroid were under twenty-five years of age. Frazell and Foote [11] showed that papillary carcinoma is the characteristic thyroid cancer of young people and children. They reported twenty-five cases of carcinoma of the thyroid gland in patients under twenty years of age, and in twenty patients the cancer was papillary. Most of these were very small in size, 15 per cent measuring under 1 cm. in greatest dimension. The point was again stressed by these authors that papillary tumors of the thyroid are of low grade malignancy and have a prolonged clinical course.

SUMMARY

Carcinoma of the thyroid usually is not suspected clinically with diffuse toxic goiter. When the association occurs, the cancer is usually small, often of the papillary type, especially in patients under twenty-five years of age. Often it is discovered only on microscopic examination of the surgical specimen. It has been established that papillary carcinomas of the thyroid are of low grade malignancy and have a prolonged clinical course. This case presented herein occurred in a seventeen year old girl with diffuse toxic hyperplasia of the thyroid in which a small papillary carcinoma was found on microscopic examination of the surgical specimen. We believe the postoperative management of such patients should be conservative and limited to periodic examinations, reserving extensive surgical removal of the regional lymphatics only when recurrence or regional lymph node metastasis becomes clinically manifest.

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Stewart-Treves Syndrome

ANGIOSARCOMA IN POSTMASTECTOMY LYMPHEDEMA ASSOCIATED WITH DISSEMINATED FIBRINOID VASCULAR LESIONS

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Primary angiosarcoma in an extremity is rare [15]. Hence, it is comprehensible that angiosarcoma of the arm as a complication of long-standing lymphedema following radical mastectomy has received prompt consideration. Stewart and Treves [17] first recognized this syndrome in 1948 and incriminated a general systemic carcinogen in the genesis of both mammary carcinoma and angiosarcoma. Perusal of the literature, however, reveals reports on angiosarcoma developing in a limb the site of long-standing lymphedema in the absence of malignancy elsewhere [1,11,12]. Thus, we are led to believe that a direct etiologic relationship exists between long-standing lymphedema and angiosarcoma [14].

Evidence has accumulated that disseminated fibrinoid vascular lesions are occasionally a characteristic histologic finding in patients succumbing to carcinomatosis [5,7]. Since the recognition of immunoallergic mechanisms in which the vascular walls represent the shock site, fibrinoid vasculopathy has attracted a great deal of attention. It is the purpose of this communication to report on fibrinoid vascular lesions accompanying the Stewart-Treves syndrome.

CASE REPORT

When she was forty-seven years of age, F. C. underwent radical mastectomy for scirrhous carcinoma located in the upper outer quadrant of the right breast. The axillary lymph nodes were not involved. Recovery was complicated by wound suppuration and purulent pleuritis. After the patient was discharged, x-ray treatment was instituted. Severe and persistent lymphedema of the right arm ensued within a few months after operation. Seven and a half years after mastectomy the patient was referred to us by her family physician, who found a painful and tender cutaneous lesion on the right arm.

On admission the patient was well nourished. The right arm was markedly swollen and edematous, and movements of the shoulder and elbow joints were hindered. On the dorsal distal aspect of the right upper arm there was a rounded, firm, slightly raised, purplish-blue plaque, about 2 cm. in diameter. It was surrounded by a halo of light purplish skin, in the periphery of which were some other similar but smaller satellite nodules. Apart from the mastectomy scar which was unaffected, general examination revealed no other significant findings. Blood pressure was within normal limits. Routine laboratory studies were noncontributory. The skin lesion was excised.

Histologic examination showed a neoplastic process involving the lower corium and subcutis. (Fig. 1B.) The overlying epidermis was slightly atrophic. The upper and mid-corium contained perivascular infiltrations consisting principally of lymphocytes and histiocytes. The collagenous connective tissue was denser and more cellular than normal. The tumor was comprised of fusiform, rounded and polygonal cells forming the lining of bizzare and variously sized vascular spaces. (Fig. 1C.) In some areas the cells were arranged in small solid masses, bundles and whorled fasciculi. The outlines of the light-staining pink cytoplasm of the tumor cells were ill-defined. The nuclei were for the most part elongated to ovoid, vesicular, with finely dispersed chromatin and prominent nucleoli. Occasional nuclei were bizzare and hyperchromatic. Mitotic figures were rare. Red blood cells were present in a few vascular channels. Blood extravasation was extensive. Scattered throughout singly and in small groups were capillary and sinusoidal vessels lined by normal appearing endothelial cells.

Although the cellular appearance varied in different parts of the growth, sections impregnated with silver revealed the majority of the tumor cells to be grouped inside of a delicate reticulin fiber

framework. Occasionally, the cells were closely packed and heaped up in the lumina, thus obscuring the vascular pattern of the tumor in the sections stained with hematoxylin and eosin. However, there were some areas in which the picture bore a strong resemblance to a spindle cell sarcoma. Connective tissue stains disclosed some newly formed, fine collagenous fibers.

A diagnosis of angiosarcoma was made. Since the patient declined amputation of the arm, she was referred for radiotherapy. In the course of the following months new lesions appeared on the upper arm and forearm and were associated with increasing pain. Spread to the chest wall and unendurable pain necessitated hospitalization. The patient was in poor general and nutritional condition. The cutaneous tumors were confluent, partly ulcerated and overlaid with serosanguineous secretion. Laboratory findings were not unusual except for an elevated sedimentation rate and a moderate anemia. Analgesics and chlorpromazine did not mitigate the pain. The patient, reduced to despair, insisted on amputation which was performed as a palliative measure.

Grossly, the arm was considerably swollen. The unaffected skin was coarse and wrinkled and had a light brownish tinge. The dermis and subcutis were indurated. The skin of the entire arm was covered with innumerable, confluent, polymorphic, variously sized, firm, slightly elevated, purplish-blue plaques, nodes and nodules, some of which were ulcerated and overlaid with hemorrhagic crusts. (Fig. 1A.) The cut surface revealed hemorrhagic tumor masses in the cutis and subcutis. These were surrounded in part by whitish tissue of fibrous appearance, and small whitish nodules were scattered throughout. The growth infiltrated through the fasciae and extended into the muscles. In some places only the deeper structures were involved.

Microscopically, the epidermis was irregularly hyperplastic, atrophic or destroyed by tumor invasion. The ulcerations were covered with necrotic debris and hemorrhagic fibrinous material. The growth was similar to the one excised eighteen months previously, but cellular anaplasia and pleomorphism were more pronounced. Mitotic figures were numerous. Extensive hemorrhage and coagulation necrosis were present. The adventitia and media of some medium-sized veins were infiltrated. A few nerve trunks were also involved; the epineurium was invaded, but the individual primary fascicles were spared. The arteries and veins of various sizes were conspicuously narrowed by fibrous intimal thickening.

The patient was discharged, but had to be admitted three months later with severe pulmonary edema. She was dyspneic and repeatedly expectorated sputum stained with blood. Her condition deteriorated rapidly and she died in a few hours.

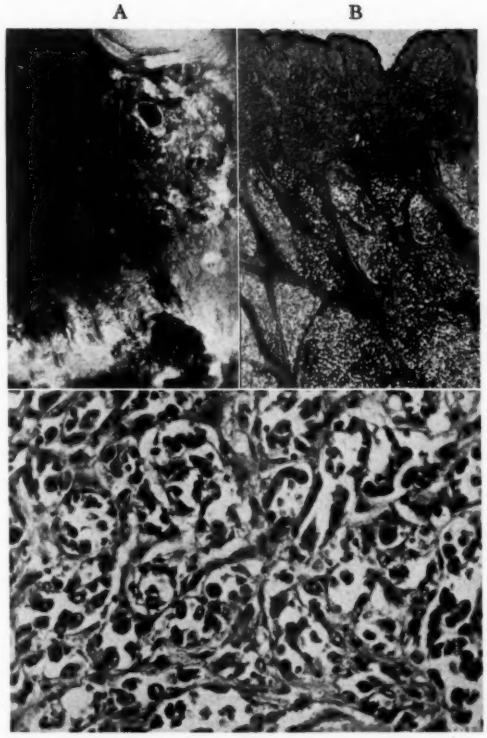

FIG. 1. A, gross photograph of swollen arm covered with a multitude of confluent, variously sized, slightly raised plaques, nodes and nodules. Some lesions are ulcerated and crusted. B, low power view of cutis and subcutis. The growth involves the lower dermis and adipose tissue. C, bizzare vascular spaces lined by an excessive number of neoplastic cells. Hematoxylin and eosin stain. Original magnification × 190.

AUTOPSY FINDINGS

The body was that of an emaciated white woman. Scars of right radical mastectomy and arm amputation were well healed. On the skin of the right axilla and chest wall there were a number of polymorphic, variously sized, firm, slightly raised, blue-purplish plaques, nodes and nodules, some of which were ulcerated and overlaid with hemorrhagic crusts. The chest wall on the right side was extensively invaded by hemorrhagic friable tumor masses which extended into and obliterated the pleural cavity. The right lung, pericardium, diaphragm and abdominal wall were infiltrated per contiguity. The cut surface of the right lung exuded a large amount of hemorrhagic frothy fluid. The left lung was edematous. The pericardial cavity contained a hemor-

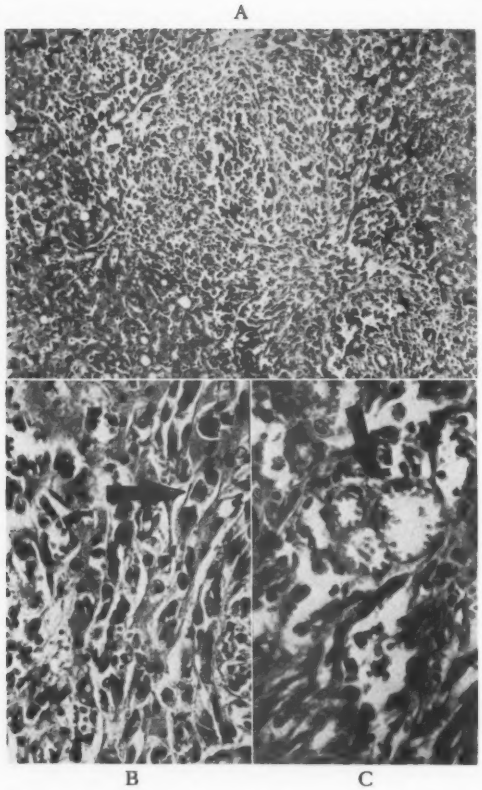

FIG. 2. A, metastatic nodule in the liver. Hematoxylin and eosin stain. Original magnification × 40. B, higher magnification of the advancing border of the hepatic metastasis. The tumor cells are replacing the sinusoidal littoral cells. Note mitotic figure in an intrasinusoidal tumor cell (arrow). Hematoxylin and eosin stain. Original magnification × 190. C, tumor tissue from the abdominal wall. There is a group of three vessels lined by normal appearing endothelial cells (arrow). Hematoxylin and eosin stain. Original magnification × 190.

rhagic effusion of about 250 ml. There was moderate atherosclerosis of the aorta and coronary arteries.

In the right lobe of the liver there were a few, small, gray-white, firm nodules, demarcated by a thin red rim from the surrounding parenchyma. The gallbladder was somewhat dilated and contained mucoid fluid; dissection of the biliary tract disclosed no obstruction. The other organs were not remarkable grossly.

The brain was pale, but otherwise normal. Lying above the pituitary fossa, a pea-sized meningioma adherent to the diaphragma sellae was found.

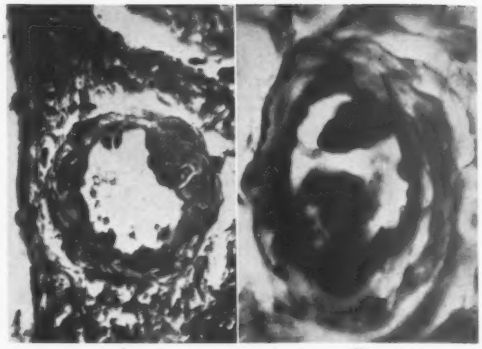

FIG. 3. A, small artery of a portal tract displaying subendothelial accumulation of smudgy eosinophilic material. × 360. Hematoxylin and eosin. B, myocardial arteriole showing subendothelial accumulation of material positive to periodic acid-Schiff staining continuous with intraluminal polypoid projections. Periodic acid-Schiff stain. Original magnification × 360.

HISTOLOGIC EXAMINATION

The tumor was similar to the surgical specimen. The ribs were surrounded by the growth, which extensively infiltrated the periosteum but only rarely eroded the cortical bone. In the marrow of a few ribs and in the fourth lumbar vertebra small metastatic foci were found. Massive replacement of the parenchyma by hemorrhagic and partly necrotic tumor tissue was seen in the right lung, but there were also infiltrated alveoli in which the alveolar septa formed the stroma of the growth. The macroscopically described hepatic nodules were metastatic angiosarcoma. (Fig. 2A.) At the advancing border the tumor cells extended amongst the liver cell cords, gradually replacing the littoral cells of the sinusoids. (Fig. 2B.) It was of interest to note that wherever angiosarcomatous tissue was present, single and small groups of capillary and sinusoidal vessels lined by normal endothelial cells were observed. (Fig. 2C.)

The liver had undergone slight centrilobular fatty metamorphosis and eosinophilic necrosis. The small arteries and arterioles of the portal tracts revealed moderate to marked subendothelial accumulation of smudgy, eosinophilic, material positive to periodic acid-Schiff staining, at times blurring the structure of the wall. (Fig. 3A.) This was either localized to a part of the circumference or encircled it completely. In continuity with the subendothelial deposits were intraluminal polypoid protrusions of the material, which was irregularly covered with and/or contained endothelial cells. (Fig. 3B.) There was no associated inflammatory infiltrate. These lesions will henceforth be referred to as "fibrinoid vascular lesions." Numerous fibrinoid vascular le-

sions were present in the heart, kidneys, periadrenal adipose tissue and intestinal submucosa. In the kidneys the afferent arterioles were particularly affected. The capillary basement membranes of most glomeruli were thickened. Sections of the other organs disclosed no additional findings of note.

COMMENTS

In recent years the Stewart-Treves syndrome is recognized with increasing frequency. McConnell and Haslam [14] found an incidence of 0.45 per cent in their material. Apparently many cases were misdiagnosed in the past as recurrences of mammary carcinoma [10]. The diagnosis should be entertained and confirmed or contradicted by biopsy if a hemorrhagic skin lesion becomes apparent in a lymphedematous arm following radical mastectomy. According to Stout [18], sarcomatous angiogenesis is characterized histologically by the "formation of atypical cells in greater numbers than are required to line the vessels with a simple endothelial membrane." The question of whether or not angiosarcoma developing in a lymphedematous limb originates in endothelial cells lining lymph or blood vessels has not been definitely settled [14]. McCarthy and Pack [12] believe that the lesion of the Stewart-Treves syndrome is structurally indistinguishable from Kaposi's sarcoma. Jessner and his associates [9] have proposed that the tumor consists of a mixture of neoplastic lymphatics and blood vessels.

The number of cases reported to date is too small for definite conclusions regarding optimal treatment. Notwithstanding the opinion that radiotherapy should be given priority [10,16], our case supports the view that this method is ineffective [8]. Since our patient declined amputation of the arm at an early phase, local excision followed by x-ray irradiation was performed. Subsequently numerous new lesions appeared which gave the impression of multicentric origin. It is, therefore, quite conceivable that a single angiosarcomatous focus in a limb the site of longstanding lymphedema denotes a precancerous state. Hence, interscapulo-thoracic amputation seems to be the only effective therapeutic measure [8,15].

In our patient the development and spread of the angiosarcoma were accompanied by pain, which gradually became unendurable and resistant to analgesics. The cause of the pain remains unknown to us. It is noteworthy that the lesion was already distressing when the patient was first referred to us and when the disease process was still restricted to the dermis and subcutis as demonstrated histologically. Involvement of the nerve trunks assuredly occurred later on. Raven and Christie [15] cite a case of a forty-four year old woman who had had elephantiasis of the right foot and leg since childhood and in whom the development of an angiosarcoma was associated with sharp shooting pain. Severe ache was experienced by the patient when a recidivation appeared after amputation. Further surgical intervention was necessary although the tumor was already unoperable.

Widespread vascular lesions of the type described in this patient occur under various pathologic conditions. The small arteries and arterioles are mainly affected, but occasionally the arteries of medium size, renal glomeruli and valvular endocardium are involved as well. Apparently the endothelium and/or subendothelium are electively damaged. The corresponding morphologic alterations are characterized by disseminated fibrinoid vascular lesions, thickened glomerular capillary basement membranes and degenerative verrucal endocardiosis [2,5]. The recent hypothesis that these manifestations represent the morphologic expression of a hypersensitivity reaction is gaining ground. One of us has studied similar vascular, renal and cardiac lesions in thrombotic thrombocytopenic purpura [4] and in congenital afibrinogenemia complicated by the formation of antibodies against infused fibrinogen [6]. Fisher and Baird [7] gave an account of two cases of fibrinoid vascular lesions in patients succumbing to carcinomatosis. In one patient it was associated with verrucal endocardiosis. It is assumed that neoplasms are capable of elaborating certain, as yet undefined, altered proteins which elicit an immunoallergic response [7]. In this immunoallergic mechanism, the vascular walls, and occasionally the glomerular capillary basement membranes and valvular endocardium, represent the shock site. McCombs and McMahon [13] postulated a similar mechanism to explain the association of dermatomyositis with carcinoma. The combination of dermatomyositis and fibrinoid vascular lesions in a patient with metastasizing ovarian cancer was recently described by Kessler from our laboratory [3].

SUMMARY

A case is presented in which angiosarcoma developed in a lymphedematous right arm

seven and a half years after radical mastectomy. Local excision and radiotherapy were followed by the appearance of new lesions and spread to the chest wall. This was accompanied by increasing pain. The patient died two months after palliative amputation of the arm. Autopsy revealed extension of the tumor to the right lung, pericardium, diaphragm and abdominal wall and metastases in the ribs, vertebra and liver. In addition, widespread fibrinoid vascular lesions and thickening of the glomerular capillary basement membranes were present.

Interscapulo-thoracic amputation of the arm is urged for angiosarcoma in postmastectomy lymphedema. The nature of fibrinoid vascular lesions associated with malignant neoplasms is discussed.

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Nodular Hyperplasia of Brunner's Glands of the Duodenum

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Hyperplasia of Brunner's glands of the duodenum is a rare finding in clinical practice. The condition has been described by pathologic anatomists since 1876. In 1934 Feyrter [8] classified hyperplasia of Brunner's glands into three types in examining 2,800 duodenums. The first classification is diffuse nodular hyperplasia. Coarse mucosal folds and irregularly circumscribed nodules composed of duodenal glands are distributed throughout the greater part of the duodenum in these cases. The second type is circumscribed nodular hyperplasia in which isolated nodules of Brunner's glands are located in the suprapapillary portion of the duodenum and often accompanied by atrophy of the intervening glands. The third is adenomatous hyperplasia in which tumor-like growths of single nodules that vary in size between that of a pea and that of a hazlenut are found. These frequently contain cystic dilatations. In 1943 Robertson [12] studied 15,000 duodenums and concurred with Feyrter's classification except that he substituted the word "hypertrophy" for hyperplasia. He also noted their wide variation in quantity and their frequent tendency to dilatation, cyst formation, and disintegration. He was the first to observe their diminution in quantity in the region of chronic and healed duodenal ulcers. Wilensky [15] stressed that the hyperplastic changes in these glands are related to their functional activity rather than a true neoplastic mechanism. This is the consensus of opinion of other investigators as well.

In a recent study of the physiology of Brunner's glands, Grossman [10] describes the alkaline mucin secretion which occurs spontaneously and is augmented by neural and hormonal factors as well as by local stimulation. Present knowledge indicates that the principal function of the juice is to protect the mucosa of the first portion of the duodenum against damage by the acid chyme from the stomach. This is accomplished by the formation of a protective coating rather than by neutralizing the acid. This function of Brunner's glands undoubtedly accounts for the clinical finding that the duodenum is probably the most resistant part of the intestinal tract to peptic ulceration [9].

At this point it might be well to comment on adenomas of Brunner's glands. This corresponds to the third type in Feyrter's classification, the solitary adenoma located usually in the duodenal bulb. They may be either sessile or pedunculated and vary in size from 0.2 to 6.0 cm. To date seventy-three cases have been reported in the literature [13]. Evidence has been accumulated to show that chronic inflammation may predispose the glands of Brunner to hyperplasia and resultant formation of adenomas [3]. Most pathologic studies have shown fibrosis, lymphocytes, and plasma cells in the region of the adenoma. These solitary tumors frequently cause symptoms. Warren [14] classifies these under the headings melena, ulcer-like distress, and motor disturbances. Hemorrhage, epigastric pain, and diarrhea may occur, but symptoms are extremely variable. The x-ray picture of a solitary filling defect (usually pedunculated) in the first portion of the duodenum should make the clinician suspicious of this lesion. Warren states that all polypoid lesions of the intestinal tract should be treated surgically. For this lesion operation consists of duodenotomy and local excision of the adenoma. Hoffman and Grayzel [11] analyzed sixty-six cases of benign duodenal tumors and

list them in the following order of frequency: adenomas, twenty-one; myomas, eleven; pancreatic rests, eight; Brunner's gland adenomas, seven; hemangiomas, five; lipomas, five; and miscellaneous, ten.

This report is concerned primarily with nodular hyperplasia of Brunner's glands, Feyrter's type two. Very few such cases have come to surgery and in all probability most are asymptomatic.

The first case in which adequate preoperative clinical and roentgen studies were done was reported by Erb and Johnson [6] in 1948. This was a thirty-six year old man who had symptoms of loose stools, secondary anemia, and slight weight loss over a one year period. Preoperative roentgenograms showed multiple polyp-like defects in the duodenal cap. The gastric analysis showed peak figures of 150 units of free hydrochloric acid and 168 units of total acid. At operation 3 inches of proximal duodenum and 3 inches of distal stomach were removed in one piece and an end to end gastroduodenostomy was performed. Within two weeks postoperatively a large marginal ulcer developed and further surgery was necessary. They felt that the high gastric acidity should have warned them that the x-ray defects were not due to polyps as achlorhydria is almost invariably present with duodenal polyposis.

The next two cases were reported by Dodd, Fishler, and Park [4] in 1953. Only the first patient was operated. He was a thirty-five year old man with intermittent ulcer-like symptoms and mild diarrhea which had persisted for several years. Roentgenograms showed the typical multiple, sessile, polypoid lesions of the first part of the duodenum. Gastric analysis showed a mild hyperacidity. This patient underwent laparotomy to rule out the possibility of true mucosal polyps. At operation only a few nodules were removed for biopsy to establish the diagnosis, and the duodenum was left *in situ*. "The acid-producing portion of the stomach was removed" and a gastro-jejunal Hoffmeister anastomosis accomplished. Their second patient complained of stomach cramps and indigestion of short duration. The serial x-ray examination of the upper gastrointestinal tract were typical of hyperplasia of Brunner's glands. Repeat gastric analyses showed elevated levels of free hydrochloric acid. This patient was not operated on but put on a regimen of antispasmodics, antacids, and bland diet. Repeat gastric analyses and roentgenograms were made and were similar to the original ones. The patient remained free of symptoms after his original attack. These authors conclude that, "the diagnosis of hyperplasia of Brunner's glands can be made when gastric hyperacidity is found in the presence of roentgenologically-demonstrable multiple duodenal nodules in a patient with a vague history of abdominal distress conforming to no specific pattern. Since this hyperplasia is thought to be a protective phenomenon against gastric hyperacidity, surgical resection of the stomach need not be carried out and more important, the duodenal tumefactions may be accepted as a benign process. It is felt that judicious use of general therapeutic measures to control symptoms and combat hyperacidity is sufficient."

The third and last reported case of hyperplasia of Brunner's glands which was surgically corrected was that of Epstein and Cole [5] in 1954. A correct preoperative diagnosis was made on their fifty-two year old male patient. This was verified at surgery by duodenotomy and biopsy. Anterior gastroenterostomy and vagotomy were carried out.

Since 1955 other cases diagnosed roentgenologically but not undergoing surgery have been reported. This condition is frequently asymptomatic and the term "duodenitis" probably has been erroneously employed for hyperplasia of Brunner's glands [1]. In a recent review of Feldman and Feldman [7], they state that preoperative diagnosis has been made in some instances but in most cases it is made postoperatively or at autopsy. Apparently the condition usually responds to medical ulcer therapy, whether or not it is correctly diagnosed roentgenologically. The following is a case diagnosed postoperatively, not suspected by x-ray, and not responding to ulcer therapy.

CASE REPORT

A fifty-three year old Negro chauffeur was admitted to Mercy Hospital on January 1, 1959. He had been in excellent health up until two months prior to admission. The symptom which caused him to seek treatment was vomiting which had occurred every day and almost invariably on arising in the morning. This was not associated with nausea but always contained some blood. Bright red streaks and, at times, clots were seen in the vomitus which was mucous-like in character. He noticed that all types of food gave him postprandial epigastric pain, gaseous eructation, and, at times, vomiting.

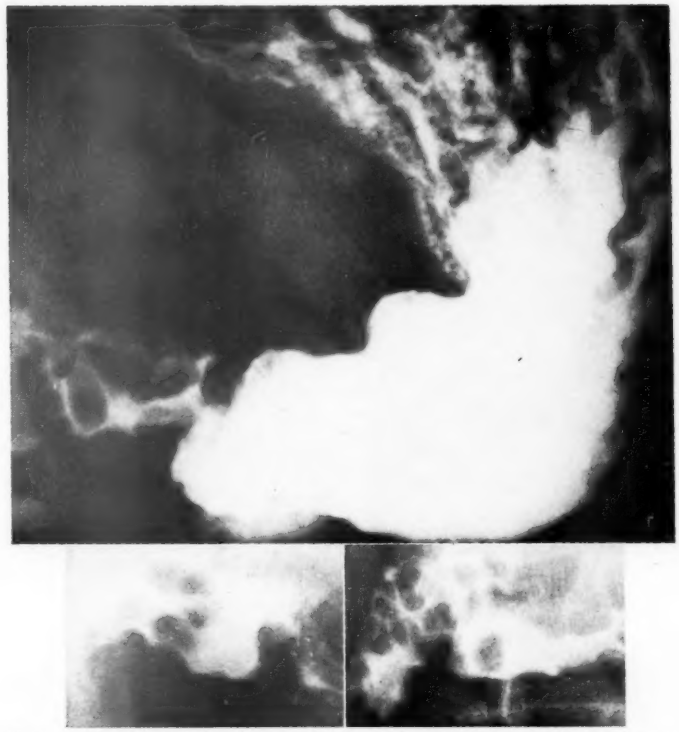

FIG. 1. Gastrointestinal series, December 20, demonstrating duodenal polyposis.

His stools occasionally were very dark, but never tarry in nature. In addition, he had lost about five pounds and complained of increasing fatigue and moderate exertional dyspnea.

On November 20, 1958, three weeks after the onset of his symptoms, roentgenograms revealed a normal upper gastrointestinal tract except for polyposis of the duodenal cap and the adjacent portion of duodenum. He was then given an ulcer regimen as an outpatient which consisted of a bland diet, probanthine, and antacids. This gave him no relief of his pain or hematemesis, and his fatiguability increased as he was afraid to eat. Another gastrointestinal series by the same radiologist on December 20 showed no change from his previous films after one month of ulcer therapy. (Fig. 1.)

History and Physical Examination. The past history was noncontributory, and there had been no previous gastrointestinal symptoms. A review of the systems was essentially negative except for a chronic cough which had persisted for six months. He stated that he smoked a half pack of cigarettes a day and did not drink alcohol in any form. Physical examination revealed a light skinned, well nourished, fifty-three year old Negro man in no acute distress The temperature was 98.8°F., the pulse was 94, and the blood pressure was 155/90 mm. Hg. His heart rhythm was regular and no murmurs were heard. A few moist rales were heard at the base of the left lung. The abdomen was rounded and there was tenderness in the epigastrium just to the right of the midline. No organs or masses could be palpated. Rectal examination was within normal limits as was the remainder of his physical examination.

Laboratory Studies. Initial hemoglobin value was 14.5 gm. per cent. The erythrocyte count was 5,060,000 per cu. mm., and the leukocyte count was 13,050 per cu. mm. Serum bilirubin was 0.6 mg. per cent. Total proteins measured 6.3 gm. per cent; blood urea nitrogen, 10 mg. per cent; blood sugar, 119 mg. per cent. The prothrombin time was within normal limits. The electrocardiogram showed moderate left axis deviation with inverted T waves in Lead II and AVF. It was reported to be within normal limits. Roentgenograms of the chest and cholecystogram revealed no defects. A second gastrointestinal series was taken on the day after hospital admission. Findings in these films were interpreted as definite

FIG. 2. Gross specimen of duodenal segment and stomach demonstrating "cobblestone" nodular hyperplasia.

ulceration in the first portion of the duodenum. Hyperplasia of Brunner's glands, duodenal polyposis, and pancreatic rests were also mentioned as possible diagnoses.

Gastric analysis was attempted but only a residual specimen was obtained for examination. This showed 16 degrees free hydrochloric acid and 30 degrees total. The test was discontinued at this point as the patient could not tolerate the tube. Although the test was incomplete, it was believed to represent a low to normal acidity.

Hospital Course. After entering the hospital the patient had no further episodes of vomiting. His treatment consisted of belladonna, phenobarbital and a bland diet.

It was believed that the patient probably had multiple benign polypoid lesions in his duodenum which were the source of his hematemesis and upper gastrointestinal symptoms. He had not responded clinically or by roentgenographic evidence to a medical ulcer regime prior to hospitalization.

On January 7 he underwent surgery. Exploration of the abdomen revealed no abnormalities except some colonic diverticula, a slightly dilated esophageal hiatus which admitted two fingers, and multiple small masses in the first portion of the duodenum. Duodenotomy was then performed and the masses more accurately palpated. One was removed for examination. The benign nature of the process was ascertained; however, it was thought to be advisable to remove all of the little tumors to prevent any possible malignant change and to divert gastrointestinal flow from the duodenum because of the preoperative bleeding. As these nodules were multiple, sessile, and occupied the entire supra-ampullary portion of the duodenum, their total removal was technically impossible through the duodenotomy. A Billroth II gastric resection was performed removing the proximal 2 inches of duodenum. The remaining nodules were locally excised through the transected duodenum. Approximately 50 per cent of the stomach was removed.

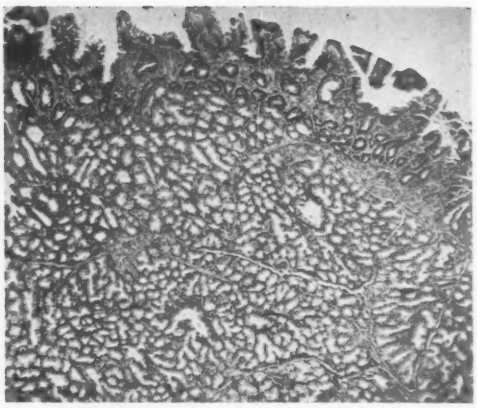

FIG. 3. Microscopic section through nodule showing hyperplasia of Brunner's glands.

Pathologic Report. The pathologic diagnosis was nodular hyperplasia of Brunner's glands of the duodenum and chronic gastritis. There was no duodenal ulcer. Scattered areas of recent submucosal hemorrhage were seen throughout the stomach segment. All the locally-excised nodules and those in the duodenal segment were composed of hyperplastic Brunner's glands. There was lymphocytic infiltration of the duodenal mucosa but no gross evidence of ulceration of the nodules. (Figs. 2 and 3.)

The patient's postoperative course was uneventful and he was discharged from the hospital thirteen days later on frequent small feedings. Three months after leaving the hospital the patient has been able to eat without distress. He experienced mild postprandial weakness for two months. He lost about fifteen pounds in weight but regained most of it. Six weeks after discharge he was able to return to his job as chauffeur.

COMMENTS

The case presented is that of a fifty-three year old man with the classical pathologic picture of hyperplasia of Brunner's glands of the first portion of the duodenum. The gross

"cobblestone" appearance was similar to that described by Erb and Johnson and the diagnosis was verified by pathologic examination after operation. The diagnosis at operation was multiple benign polyps of the duodenum. In retrospect, there probably was no need to remove all these polypoid masses; one for diagnosis would have sufficed as malignant degeneration of the lesions has rarely, if ever, been verified. The performance of a Billroth II hemigastrectomy is still thought to be the operation of choice in the light of this patient's symptoms, namely, hematemesis, postprandial distress, and failure to respond to a medical ulcer regime. Certainly the failure to perform a complete preoperative gastric analysis is regrettable as this might influence the extent of gastrectomy performed and the possible advisability of vagotomy.

SUMMARY

1. The pathologic types of hyperplastic changes in Brunner's glands of the duodenum are presented and their etiology and function are discussed.

2. Nodular hyperplasia of Brunner's glands produces no pathognomonic symptoms but should be suspected in the presence of roentgen findings of multiple sessile tumefactions in the first portion of the duodenum usually accompanied by a gastric hyperacidity.

3. This condition is totally benign, probably inflammatory, and usually responds to medical treatment of antacids and antispasmodics.

4. When operation is required because of persistent symptoms or to establish the diagnosis, the surgical procedure performed must be individualized depending on the nature of the symptoms.

5. A case of nodular hyperplasia of Brunner's glands treated by Billroth II hemigastrectomy with removal of the nodules is presented.

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CASE ANALYSIS CLINIC

Nonopaque Ureteral Calculus

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PATIENT E. C., a thirty-nine year old sales engineer, was in good health until four hours prior to admission to the hospital. While sitting at his desk three hours after his morning meal, he experienced an acute onset of left sided colicky pain. The pain originated in the high lumbar area and radiated around the left flank into the left side of the lower abdomen and the left side of the scrotum. The pain was described as excruciating and paroxysmal. The patient became nauseated, weak and pale and perspired freely. He consulted the physician at the plant who partially relieved the pain by administration of ½ gr. of morphine sulfate. Following examination, including complete blood count and urinalysis, the patient was transferred to the Urological Service at this hospital.

PHYSICAL EXAMINATION

The patient was a slightly obese white man in no acute distress but complaining of mild aching pain in the left flank and nausea. He was afebrile with a pulse of 100 per minute. Abdominal examination revealed some tenderness to palpation in the left costovertebral angle and left flank. Bowel sounds were present but hypoactive. The remainder of the examination was not remarkable.

LABORATORY DATA

Complete blood count was normal; urinalysis showed numerous red blood cells and 24 to 30 white blood cells per high power field; blood urea nitrogen was 20 mg. per cent; calcium was 9.9 mg. per cent; phosphorus was 4.3 mg. per cent; uric acid was 4.7 and 5.1 mg. per cent. Intravenous pyelogram showed a normal right upper urinary tract and a mild left hydronephrosis and hydroureter with only the upper one-third of the left ureter visualizing. No calculi were seen. On the next day, following another bout of severe left renal colic, intravenous pyelogram failed to show excretion of dye by the left kidney.

EARLY MANAGEMENT

The patient was treated initially with Demerol® hydrochloride 150 mg. and atropine 0.3 mg. every three hours as needed for pain. Supplemental intravenous dextrose in water was administered to maintain fluid intake over 3,000 cc. per twenty-four hours. Urine was strained in search of calculi. Furadantin,® 100 mg. every six hours, was administered.

After the patient had remained free of pain for twelve hours, he had a second and third episode of severe left renal colic. These episodes were controlled with large doses of narcotics. Shortly after the third episode a ureteral catheter was placed in the left upper urinary tract. Approximately 100 cc. of clear urine was drained. The patient's symptoms disappeared. No manipulation was undertaken. The catheter was removed in forty-eight hours and the patient remained free of symptoms for an additional twelve hours. He then experienced his fourth and most severe episode of colicky pain in the left flank and lower abdomen. Examination of the urine revealed gross hematuria without evidence of infection.

Retrograde pyelography showed the lower two-thirds of the left ureter to be normal. The catheter met an obstruction at the junction of the upper and middle thirds of the ureter and the retrograde flow of dye outlined the caudal

aspect of the obstruction. It appeared to be round and smooth, apparently filling the lumen of the ureter.

At operation, through a muscle-splitting incision in the left flank, a hard, eroded, yellow-brown calculus was removed from the left ureter. It measured 1 cm. in diameter. No splinting or internal drainage of the ureter was carried out. Postoperative course was uneventful and the patient was discharged on the sixth postoperative day. Urine at that time was clear and intravenous pyelography performed since that time has shown a normal upper urinary tract bilaterally.

COMMENTS

The calculus weighed 118 mg. and was composed entirely of uric acid as shown by chemical analysis. Pure uric acid calculi are noted infrequently. In large calculi a nidus of uric acid surrounded by layers of carbonates and phosphates is often revealed. Calculi composed of uric acid and those of xanthine and cysteine are radiolucent.

Uric acid is a normal excretory product of the kidney, amounting to 0.4 to 0.7 gm. in a twenty-four hour specimen. It is usually present in the urine in the form of the various urates. Derangement of the purine metabolism leads to increased excretion of uric acid, a prerequisite to the creation of the "gouty kidney" or uric acid renal calculi. The latter often grow to considerable size in the renal pelvis without causing difficulty. Acute symptoms occur when a calculus falls into the ureter, which passes the calculus into the bladder. Partial or complete obstruction of the ureter brings about an easily recognizable syndrome.

Diagnosis and subsequent treatment are somewhat complicated because the radiolucency of these calculi makes it difficult to determine the position, size and surface characteristics. Complete investigation is mandatory because unexplained ureteral colic is often due to nonopaque calculus. Retrograde pyelography in this instance offers the most information. The drawbacks of this diagnostic measure are as follows: (1) the reflux and loss of the calculus into the kidney pelvis and (2) the possible introduction of infectious organisms into stagnant urine with subsequent sepsis.

Treatment of ureteral calculi has three main aspects as follows: (1) symptomatic treatment with spontaneous passage; (2) cystoscopic and catheter manipulation and extraction; (3) open operation. Various reports advocate each of these means of treatment in certain circumstances. It is agreed that calculi less than 4 mm. in diameter will pass spontaneously through a healthy urinary tract. With medium sized calculi (4 to 6 mm. in diameter) spontaneous passage occurs less frequently and only with much difficulty and attendant morbidity.

Advocates of cystoscopy with catheter extraction present evidence to support this method of removing all but large calculi; many procedures are described. It is the belief in this clinic that this method is desirable only with smaller calculi and only those that are easily reached in the lower one-third of the ureter. In most cases when spontaneous passage does not occur open operation is indicated. For calculi in the extreme upper limits of the ureter a nephrectomy incision is used. For those in the middle one-half of the ureter a muscle-splitting incision is made in the flank. For those in the lower one-third of the ureter either a McBurney or Gibson approach is recommended. Retroperitoneal exposure of the ureter is carried out. A longitudinal incision is made in the ureter and the calculus is removed. Following loose closure of the ureter with No. 4–0 chromic catgut a small drain is left in the retroperitoneal space for forty-eight to seventy-two hours. With this type of treatment, hospital stay is shortened, the pathologic condition is remedied and morbidity from infection and ureteral damage is decreased. The one prerequisite for this mode of therapy is accurate location of the calculus with the operative incision conforming to this position.

With all cases of renal calculi, appropriate metabolic studies are undertaken to define the precipitating factors and to institute prophylactic measures as indicated.

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The Diagnostic Corner

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An interesting case demonstrating the importance of radiographic technic in the study of gallbladder disease.

THIS patient, a thirty-four year old white woman, was admitted to the Ohio State University Hospital on January 21, 1956, for the third time, complaining of a severe attack of pain in the right upper quadrant which usually began in the right posterior part of the chest and radiated anteriorly under the right costal margin to the right upper quadrant and epigastrium. These pains occurred three or four hours after meals and were accompanied by severe nausea and vomiting. There was no history of jaundice, choluria, acholic stools, diarrhea, constipation or gastrointestinal bleeding. Practically all vegetables and chocolate seemed to precipitate these episodes of pain.

The patient had had abdominal surgery elsewhere for an ectopic pregnancy in August, 1943. In June, 1944, the patient was admitted to the University Hospital for the first time because of severe dysmenorrhea and eventually had a supravaginal hysterectomy and right oophorectomy for this condition. The patient was admitted to the University Hospital for the second time in December, 1955, at which time she complained of an attack of severe pain located in the region of the right lower scapula and in the epigastrium. The first such attack had occurred in October, 1955. The pain was relieved by sitting up and by vomiting. In November, 1955, the patient had two cholecystograms taken at other institutions and these roentgenograms were reported as normal.

Physical examination at the time of the third admission showed the patient to be in no particular distress. The abdomen was soft; there were two scars from the previous surgery, one in the right lower quadrant and one in the midline. No organs could be palpated. There was slight tenderness to deep palpation just to the right of the umbilicus. This tenderness was inconstant and disappeared when the patient's attention was directed to other areas. The red blood cell count was 4.25 million per cu. mm., hemoglobin 12.4 gm. per cent, white blood cell count 9,000 per cu. mm. with 13 per cent nonsegmented polymorphonuclear leukocytes, 45 per cent segmented polymorphonuclear leukocytes, 35 per cent lymphocytes and 2 per cent monocytes. All other laboratory studies were within normal limits. A cholecystogram was taken in the prone position which is shown on the facing page. *What is your diagnosis?*

Please turn page for answer

Diagnosis: Multiple tiny radiolucent gallstones.

The history in this case is typical of multiple attacks of biliary colic. Even though the two previous cholecystograms taken elsewhere had been reported as "normal," it is probable that only the conventional recumbent technics had been used. On films taken in a recumbent position the x-ray beam is directed from above the patient enface at right angles to the plane of a very thin layer of tiny gallstones. This is the reason that tiny gallstones frequently are not visible on films taken in the ordinary recumbent position with a vertical x-ray beam. However, if a horizontal x-ray beam is used with the patient in the upright or lateral decubitus position, the beam strikes the layer of tiny radiolucent gallstones tangentially with the result that they can be clearly seen. The use of the horizontal beam technic is fast becoming a popular method throughout many radiology departments. The use of these technics has resulted in a much higher percentage of positive diagnoses in cases in which tiny radiolucent gallstones would not be noted on ordinary recumbent technics with vertical x-ray beams.

At surgery many adhesions were encountered throughout the abdomen, apparently due to the previous surgical procedures. The wall of the gallbladder was moderately thickened and slightly inflamed. There were many tiny gallstones measuring 1 to 3 mm. in diameter. The gallbladder was removed without difficulty. No stones were encountered in the common duct or cystic duct at the time of surgery. The patient made an uneventful recovery and has had no recurrence of her preoperative symptoms.

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Surgery Court Cases

HOWARD NEWCOMB MORSE,* *Atlanta, Georgia*

ROBERTSON VS. COPELAND

Supreme Court of Mississippi

97 So. 2d 512

This was a malpractice action. The Circuit Court of Hinds County, Mississippi, directed a verdict in favor of the surgeon; the patient appealed. The surgeon had performed a complete hysterectomy on the patient, who had suffered subsequent complications. The patient claimed that the operation should not have been performed at all at the time it was performed.

The hospital records and the testimony of the surgeon on the one hand, and the testimony of two other surgeons who testified as expert witnesses for the patient on the other hand were in utter conflict on a number of the material points at issue. In such a situation, according to the Supreme Court of Mississippi, the case is a proper one for submission to the jury.

The Supreme Court, therefore, reversed the decision of the lower court and remanded the case to that court for a new trial. The Supreme Court declared: " . . . we think that there is ample conflicting testimony . . . as to whether or not the operation performed by the defendant should have been performed at all at the time it was performed . . . therefore the trial court was in error in directing a verdict in favor of the defendant and thereby withholding from the jury a decision of the material issues involved."

MONDOT VS. VALLEJO GENERAL HOSPITAL AND JONES

District Court of Appeal of California

313 P. 2d 78

This was an action for damages alleged to have been caused by the negligence of a surgeon in that in the course of the operation the surgeon negligently and carelessly lost and left in the patient's body a piece of rubber, plastic or foreign material. The Superior Court of San Diego County, California, directed a verdict for the hospital and surgeon; the patient appealed.

The patient, at the request of her family physician (not the operating surgeon), entered the Scripps Metabolic Clinic at La Jolla, California, for a physical examination. After examination and study, the clinic reported she was suffering from an ovarian deficiency due to some pelvic inflammatory process, then quiescent.

The patient was admitted to the Vallejo General Hospital, where the surgeon performed an abdominal operation to correct the position of her uterus and to free adhesions. Complications subsequently ensued and the patient entered the Chulu Vista Hospital where a second surgeon reported that in his examination he noted that she had a cyst on the adnexa. The cyst, which the second surgeon removed, was the size of a small orange and contained a piece of foreign matter approximately one and a half inches long, a half inch wide and an

* Counsellor at Law of the Supreme Court of the United States of America.

eighth inch thick. A third surgeon, who assisted the second surgeon in the operation, testified that he thought it was a piece of either glove, rubber or rubber tube, but was not positive that it was rubber. Following the operation of removing the cyst, the patient's health improved. The patient testified that from the time of the abdominal operation until removal of the foreign matter she had undergone much pain; however, after the removal of the foreign material she no longer suffered this pain.

The patient contended that the lower court erred in instructing the jury to return a verdict in favor of the Vallejo General Hospital and the surgeon who had performed the abdominal operation. The District Court of Appeal of California agreed with this contention, reversing the decision of the trial court. The District Court of Appeal stated: "Considering the evidence herein . . . in the light most favorable to . . . (the patient) . . . we cannot hold that there is no evidence of sufficient substantiality to support a verdict in favor of . . . (the patient) if such a verdict were given."

BOOK REVIEWS

Multilingual Manual for Medical Interpreting, Louis R. M. Del Guercio, M.D. 160 pages. Pacific Printing Company. New York, 1960. *$2.50.*

The problem of communication between physicians in the United States and patients who cannot speak English has increased since the study of languages has not kept pace with world travel. The doctor who can approach a foreign-born patient in his native tongue gains the patient's respect and trust more easily. *The Multilingual Manual for Medical Interpreting* was compiled with this thought in mind. It is a handbook with which the physician in the United States who has not studied foreign languages can question and examine patients in six languages (French, Spanish, German, Italian, Polish and Russian). Most of the 100 subdivided statements and questions can be answered yes or no. The simple system of phonetics utilizes English syllables and can be read at a glance. It is unlikely that even the most blundering attempts at pronunciation would elicit ridicule from patients who are usually relieved and happy to hear their doctor use their native language. Of course it is possible to point to the literal translation so that the patient may read the question for himself.

The manual is well organized and attractive, and it is assumed that the few typographical errors will be corrected in future editions. It is also hoped that other languages such as Yiddish, Hungarian and Portugese will be added.

This book is recommended for use by doctors at all levels, and clinical clerks should be required to use it to avoid an inadequate medical history due to the language barrier. Interpreters, when available, can lead to confusion and a loss of rapport. The members of the medical profession have always been considered well educated men, and one of the marks of a good education is still the ability to transcend national boundaries through language. *The Multilingual Manual for Medical Interpreting* will not produce linguists overnight, but its use with patients who cannot speak English will certainly improve patient care and the doctor-patient relationship.

ROBERT TURELL, M.D.

Cancer, Volume 5. Part IX: Radiotherapy. Edited by Ronald W. Raven, O.B.E. (Mil.), T.D., F.R.C.S. 406 pages. Butterworth & Co., Ltd. London, 1959.

Many surgeons have only a limited knowledge of radiation therapy, yet surgeons today treat increasing numbers of cancer patients and therefore should be familiar with the methods of radiotherapy.

Any physician who wishes a speaking or working knowledge of the subject will do well to consult this text. It is complete, organized and well written, and easy to read. It appears to be a good reference for the nonradiotherapist as well as for the therapist.

Part of the book deals with basic information beginning with the historical background of radiation. The authors then discuss physical and biological properties of radiation and the basis for therapy. Methods for calculation of dosage and administration of the various radiation materials including isotopes are listed, together with the manner in which persons administering radiation are protected.

The remainder of the book concerns specific tumors and sites with clinical features, plan of treatment, dosage and technic, various types of radiation available, results of treatment and complications.

The text is practical for the general practitioner, surgeon or radiation therapist who is treating cancer.

RICHARD C. MCPHERSON

Ciba Foundation Symposium on Regulation of Cell Metabolism. Edited by G. E. W. Wolstenholme, M.B., B.CH. and Cecilia M. O'Connor, B.SC. 387 pages. Little, Brown & Co. Boston, 1959. *$9.50.*

A well selected symposium board has presented in this volume an over-all review of a complicated subject, the nature of cell metabolism. Aimed specifically at the metabolist, this informative session greatly increases the knowledge and unity of those in this complex field. Although difficult reading for the general reader, the material is presented in a clear, informed fashion.

FOSTER MARSHALL, M.D.

Anatomy for Surgeons, Volume 3: The Back and Limbs. By W. Henry Hollinshead, PH.D. 901 pages. Paul B. Hoeber. New York, 1959. *$23.50.*

The writing of an anatomy text for the specific use of surgeons requires vast knowledge of both surgery and anatomy. In this case the author is an anatomist but his data have been subjected to painstaking, detailed criticism and editing by excellent men in the surgical profession.

Although the wealth of detail will perhaps not suit the medical student, this is an excellent reference for the reader who deals in these areas.

Compared to other texts of the general gross anatomy, the careful attention to detail presented here is striking; for example, in the section devoted to the anatomy of the foot, close attention is given the bones and ligaments of the area and their relationship to a surgical problem.

FOSTER MARSHALL, M.D.

A Method of Anatomy, 6th Edition. By J. C. Boilean Grant, M.C., M.B., CH.B. 879 pages. Williams & Wilkins Co. Baltimore, 1958. *$11.00.*

This volume, now in its sixth edition, is intended primarily for the anatomist but also provides, in a clear, narrative style, a basic reference which would be applicable at all levels of medical education. Explanations are simple and descriptive. Material covers the over-all picture of the body and then goes into the history, variations, functions and uses of specific anatomic areas.

FOSTER MARSHALL, M.D.

Symposium on Glaucoma. (Transactions of New Orleans Academy of Ophthalmology.) Edited by William B. Clark, M.D. 314 pages. C. V. Mosby Co. St. Louis, 1959. *$13.50.*

This small volume summarizes current concepts of the pathogenesis and management of glaucoma. A great many practical points are emphasized. The text is readable and interesting, and it can be recommended as a good review of the subject.

WILLIAM H. HAVENER, M.D.

The Treatment of Bronchial Neoplasms. By Robert R. Shaw, M.D., Donald L. Paulson, M.D. and John Lester Kee, Jr., M.D. 135 pages. Charles C Thomas. Springfield, Ill., 1959. *$8.00.*

This is the third publication in the John Alexander Monograph Series. The authors use their experience in treating 1,180 patients with bronchogenic carcinona to present a sensible approach to this disease of increasing incidence. They challenge the long-taught classic temporal theory of tumor growth and offer a theory of biologic predeterminism. This latter theory explains why radical surgery is not necessarily the best treatment for every patient with bronchogenic carcinoma. Some lesions may be early biologically but late chronologically. Similarly the slow growth of highly differentiated squamous cell carcinomas points to prolonged survival even after surgery has been delayed. The fact is stressed that it is not just the length of survival that counts but how the patient survives. In this respect, the authors prefer lobectomy over pneumonectomy as the treatment of choice when the pathologic condition permits.

The history and natural course of thirty-five patients with bronchial adenomas is presented concisely by the third author, along with surgical technics to preserve pulmonary function without compromising chances for cure.

All physicians dealing with such patients should welcome this small monograph which serves to answer most questions arising in the care of patients with bronchogenic neoplasms.

CHARLES MECKSTROTH, M.D.

Biopsy Manual. By James D. Hardy, M.D., James C. Griffin, Jr., M.D. and Jorge A. Rodriguez, M.D. 150 pages. W. B. Saunders Co. Philadelphia, 1959. *$6.50.*

This book not only deals with the important facets of taking a biopsy specimen from many areas of the body but also describes the lymphatic drainage from these areas and in some instances outlines further therapy. Deep-seated lesions, such as mediastinal and pancreatic, are included. Noted to be absent was needle biopsy of the thyroid gland which many surgeons advocate. Although some of these biopsy procedures can be classified as major surgery, the book will be of considerable value to the young resident in general surgery both from the standpoint of technic and from the accompanying comments on indications and sequelae.

CHARLES MECKSTROTH, M.D.

A Practice of Thoracic Surgery. By A. L. d'Abreu, O.B.E., CH.M., F.R.C.S. 619 pages. Williams & Wilkins Co. Baltimore, 1958. *$19.00.*

This single volume represents one of the most complete treatises on all aspects of thoracic

surgery available today. Although only a bit over 600 pages in length, all facets of pulmonary surgery are undertaken, including anatomy, lung function, anesthesia, and a practical discussion of congenital and acquired heart disease. Bronchogenic carcinoma, tuberculosis and pyogenic infections are similarly handled with typical British thoroughness. The book is a storehouse of knowledge, rarely found in one man's experience. The paucity of contributory authors produces a continuity of thought and treatment which cannot be achieved in books of collected works. The practical aspects of treatment are paramount, based on fundamental physiology.

In the fast-changing field of open heart technics and equipment, this book, as any other, is obviously outdated and inadequate. I failed to find adequate stress placed on the importance of continuous high-negative pressure application to the pleural space immediately after thoracotomy in procedures in which large surfaces of raw lung tissue remain. Some of the photographs taken at surgery could be better explained or replaced by line drawings. The reproduction of x-ray films is positive rather than negative, which could be confusing to one familiar with the latter form. Equipment such as artificial pneumothorax apparatus and continuous suction mechanisms appear obsolete to the surgical resident of today.

In spite of these apparent drawbacks, the book is expertly written, easy to read, and provides an excellent textbook for the young thoracic surgeon who can profit from the continuity of a single man's experience in this wide and ever changing field of surgery.

CHARLES MECKSTROTH, M.D.

BOOKS RECEIVED FOR REVIEW

All books received will be acknowledged in this column. Insofar as possible, as space permits, books of special interest will receive more extensive reviews.

Manual of Applied Nutrition. Janette Carlsen. Fourth edition, 134 pages. The Johns Hopkins Press. Baltimore, 1959. *$3.00.*

Diagnosis and Treatment of Tumors of the Chest. Edited by David M. Spain, M.D. Sponsored by the American College of Chest Physicians. 371 pages. Grune & Stratton, Inc. New York, 1960. *$14.75.*

Surgical Philosophy in Mass Casualty Management. Warner F. Bowers, M.D., PH.D. and Carl W. Hughes, M.D. 204 pages. Charles C Thomas. Springfield, Ill., 1960. *$6.75.*

Intussusception in Infants and Children. Mark M. Ravitch, M.D. 121 pages. Charles C Thomas. Springfield, Ill., 1959. *$9.00.*

Handbook of Physiology. Section 1: Neurophysiology, Volume 2. Edited by John Field and H. W. Magoun. 658 pages. Williams & Wilkins Co. Baltimore, 1960. *$20.00.*

A Practical Guide to General Surgical Management. Julian A. Sterling, M.D. 67 pages. Vantage Press. New York, 1960. *$3.00.*

Medical Radioisotope Scanning. 266 pages. International Atomic Energy Agency. U. S. agent: National Agency for International Publications, Inc. New York, 1959. *$4.00.*

A Textbook of Gynecology. Laman A. Gray, M.D. F.A.C.S., F.A.C.O.G. 470 pages. Charles C Thomas. Springfield, Ill., 1960. *$15.50.*

Somatosensory Changes After Penetrating Brain Wounds in Man. Josephine Semmes, Sidney Weinstein, Lila Ghent and Hans-Lukas Teuber. 91 pages. Harvard University Press. Cambridge, Mass., 1960. *$4.00.*

Cosmetic Surgery. Principles and Practice. Samuel Fomon, M.D. 651 pages. J. B. Lippincott Co. Philadelphia, 1960. *$27.50.*

Fundamental Techniques of Plastic Surgery and Their Surgical Applications. Ian A. McGregor, M.B., F.R.C.S., F.R.F.P.S., 244 pages. Williams & Wilkins Co. Baltimore, 1960. *$7.00.*

Outline of Orthopaedics. John Crawford Adams, M.D., F.R.C.S. Third edition, 440 pages. Williams & Wilkins Co. Baltimore, 1960. *$8.00.*

Surgery of Repair as Applied to Hand Injuries. B. K. Rank, C.M.G., M.S., F.R.C.S., F.R.A.C.S. and A. R. Wakefield, M.S., F.R.C.S., F.R.A.C.S. Second edition, 284 pages. Williams & Wilkins Co. Baltimore, 1960. *$9.00.*

Pediatric Anesthesiology. M. Digby Leigh, M.D. and M. Kathleen Belton, M.D. in collaboration with George B. Lewis, Jr., M.D. and Edward B. Scott, M.D. Second edition, 461 pages. The Macmillan Co. New York, 1960. *$12.00.*

Patterns of Professional Education. William J. McGlothlin. 288 pages. G. P. Putnam's Sons. New York, 1960. *$6.75.*

Cardiac Auscultation Including Audio-Visual Principles. Second revised and enlarged edition, 102 pages.

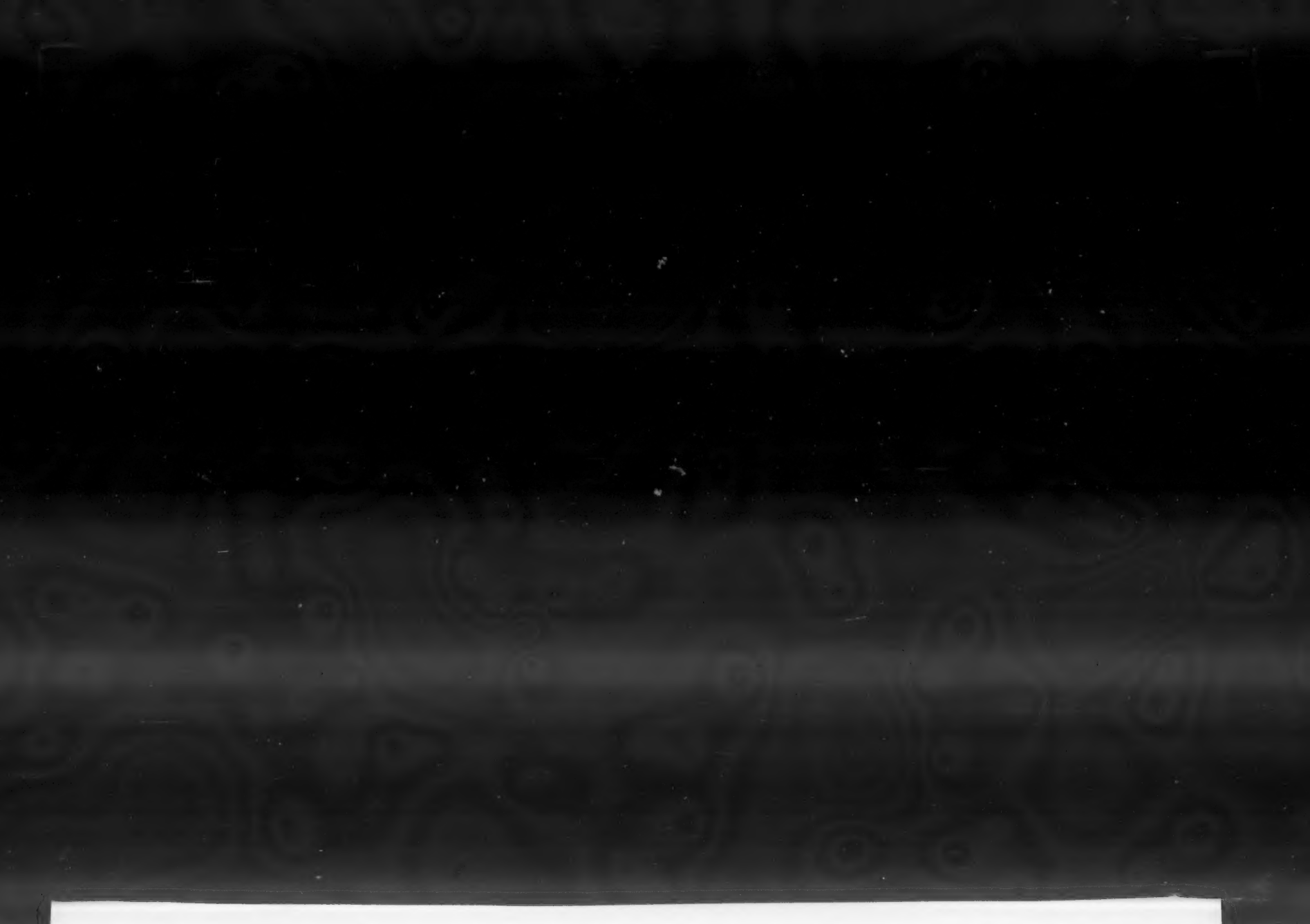
Book Reviews

J. Scott Butterworth, M.D., Maurice R. Chassin, M.D., Robert McGrath, M.D. and Edmund H. Reppert, M.D. Grune & Stratton. New York, 1960. *$6.25.*

A Catalogue of the Portraits and Other Paintings, Drawings and Sculpture in the Royal College of Surgeons of England. William LeFanu, Librarian of the College. 119 pages. Williams & Wilkins Co. Baltimore, 1960. *$6.75.*

Antithrombotic Therapy. Paul W. Boyles, M.D. 131 pages. Grune & Stratton. New York, 1959. *$5.00.*

Principles of Orthopaedic Surgery. Revised edition, 799 pages. Paul C. Colonna, M.D. Little, Brown & Co. Boston, 1960. *$22.00.*

Virus Virulence and Pathogenicity. Ciba Foundation Study Group, No. 4. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P. and Cecilia M. O'Connor, B.SC. 114 pages. Little, Brown & Co. Boston, 1960. *$2.50.*

Cancer of the Cervix, Diagnosis of Early Forms. Ciba Foundation Study Group, No. 3. 114 pages. Little, Brown & Co. Boston, 1960. *$2.50.*